subcutaneous immune globulin (SCIG)

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: IMMUNOLOGICAL AGENTS
Mechanism of Action: Immune globulin is a sterile, nonpyrogenic solution of globulins containing many antibodies normally present in adult human blood.
HCPCS:
J1551:Injection, immune globulin (cutaquig), 100 mg
J1555:Injection, immune globulin (cuvitru), 100 mg
J1558:Injection, immune globulin (xembify), 100 mg
J1559:Injection, immune globulin (hizentra), 100 mg
J1561:Injection, immune globulin, (gamunex-c/gammaked), non-lyophilized (e.g., liquid), 500 mg
J1569:Injection, immune globulin, (gammagard liquid), non-lyophilized, (e.g., liquid), 500 mg
J1575:Injection, immune globulin/hyaluronidase, (hyqvia), 100 mg immunoglobulin
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, 8gm, 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 (single use vials)

Condition(s) listed in policy (see coverage criteria for details)

- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Variants
- Chronic inflammatory demyelinating polyneuropathy (CIDP)-HOME SETTING ONLY
- Primary Immune Deficiency Disorder (PIDD)-HOME SETTING ONLY
- Primary Immunodeficiency Disorders (PIDD)

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a

prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Variants

Meets medical necessity if all the following are met:

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
2. Diagnosis by a neurologist
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
4. Motor or sensory dysfunction of more than 1 limb developing over at least 2 months
5. Absent or reduced tendon reflexes in affected limbs or gait ataxia
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

Chronic inflammatory demyelinating polyneuropathy (CIDP)-HOME SETTING ONLY

Meets medical necessity if all the following are met:

Requirements listed within the Local Coverage Determination (LCD) L33794 for subcutaneous immune globulin (SCIg)

Covered Doses:

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

Coverage Period:
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 Immune Deficiency Disorder (PIDD)-HOME SETTING ONLY
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L33794 for subcutaneous immune globulin (SCIg)

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

Initial weekly dose = 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, D80.2, D80.3, D80.4, D80.5, D80.6, D80.7, D81.0, D81.1, D81.2, D81.5, D81.6, D81.7, D81.82, D81.89, D81.9, D82.0, D82.1, D82.4, D83.0, D83.1, D83.2, D83.8, D83.9, G11.3

Primary Immunodeficiency Disorders (PIDD)

Meets medical necessity if all the following are met:

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
2. ONE of the following:
   a. IgG <200 mg/dL,
   b. All or the following:
      i. Member has a history of recurrent bacterial infections
      ii. Inability to respond to IgG antibody production after antigenic challenge against diphtheria and tetanus toxoids or pneumococcal polysaccharide vaccine
      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
Initial weekly dose = 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, D81.6, D81.7, D81.89, D81.9, D82.0, D82.1, D82.3, D82.4, D83.0, D83.1, D83.2, D83.8, D83.9

Additional Information

Summary of Evidence
The contents of this policy were created after examining the following resources:

1. The prescribing information for Cutaquig, Cuvitru, Gammagard, Gammaked, Gamunex-C, Hizentra, HyQvia, Xembify
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text

c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A" (cancer indications only)
e. Clinical Pharmacology - supportive narrative text (cancer indications only)

3. Local Coverage Determination (LCD): L33794 External Infusion Pump
4. 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 (2021)
5. American Academy of Allergy, Asthma, and Immunology (AAAAI)/American College of Allergy, Asthma, and Immunology (ACAAI), and Joint Council of Allergy, Asthma, and Immunology (JCAAI): Practice parameter for the diagnosis and management of primary immunodeficiency (2015)
6. Work Group Report of the American Academy of Allergy, Asthma & Immunology (AAAAI): Update on the use of immunoglobulin in human disease: A review of evidence (2017)
7. Human Inborn Errors of Immunity: 2019 Update on the Classification from the International Union of Immunological Societies Expert Committee

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Cutaquig, Cuvitru, Gammagard, Gammaked, Gamunex-C, Hizentra, HyQvia, Xembify are covered in addition to the following:

- Chronic inflammatory demyelinating polyneuropathy (CIDP) and variants

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- European Academy of Neurology/Peripheral Nerve Society supports use of subcutaneous immunoglobulin (SCIg) as a maintenance treatment option in IVIg-responsive CIDP patients with active disease (strong recommendation)

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS®. Available by subscription at http://www.lexi.com
5. 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.
6. Cutaquig® (immune globulin subcutaneous, human) [Prescribing Information]. Paramus, NJ: Octapharma USA, Inc.; 11/2021.
7. Cuvitru® (immune globulin subcutaneous, human) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 3/2023.
8. DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
9. Hizentra® (immune globulin subcutaneous, human) [Prescribing Information]. Kankakee, IL: CSL Behring LLC; 4/2023.
10. Gammagard® (immune globulin, human) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 1/2024.

11. Gammaked® (immune globulin, human) [Prescribing information]. Fort Lee, NJ: Kedrion Biopharma, Inc.; 6/2018.
12. Gamunex-C® (immune globulin, human) [Prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; 1/2020.
13. HyQvia® (immune globulin 10% subcutaneous with recombinant human hyaluronidase) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 1/2024.
14. LCD L33794: External Infusion Pumps
15. 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.
16. 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.
17. 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.
18. Xembify® (immune globulin subcutaneous, human) [Prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; 8/2020.

Review History

Date of Last Annual Review: 2Q2024
Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee