Immune Globulin Subcutaneous
Medicare Advantage Medical Policy #MA-199
Original Effective Date: 04/01/2026
Current Effective Date: 04/01/2026

Policy:	**Immune Globulin Subcutaneous Utilization Management Medical Policy** • Cutaquig® (immune globulin subcutaneous 16.5% solution – Pfizer) • Cuvitru™ (immune globulin subcutaneous 20% solution – Baxalta/Takeda) • Gammagard Liquid® (immune globulin infusion 10% solution – Baxalta/Takeda) • Gammaked™ (immune globulin injection 10% caprylate/chromatography purified – Kedrion Biopharma) • Gamunex®-C (immune globulin injection 10% caprylate/chromatography purified – Grifols) • Hizentra® (immune globulin subcutaneous 20% liquid – CSL Behring) • HyQvia® (immune globulin infusion 10% with recombinant human hyaluronidase – Baxalta/Takeda) • Xembify® (immune globulin subcutaneous 20% solution – Grifols)
Date:	06/17/2025
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States/Territories:	Novitas JH – Colorado, New Mexico, Oklahoma, Texas, Arkansas, Louisiana, Mississippi Novitas JL – Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania
Applicable NCDs, LCDs, and/or LCAs	NCD 250.3, L35093, A56786

SUMMARY OF EVIDENCE
Immune globulin subcutaneous (SCIG) products are concentrated human immunoglobulins, primarily immunoglobulin G (IgG), that are prepared from pooled plasma collected from a large number of human donors. SCIG products are indicated for the following uses:

- **Chronic inflammatory demyelinating polyneuropathy,** for maintenance therapy in adults.[1,4,5]
- **Primary humoral immune deficiency (PID**), for replacement therapy, including but not limited to the humoral defect in the following conditions: common variable immunodeficiency, X-linked agammaglobulinemia (congenital agammaglobulinemia), Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.[1-5,7-9] SCIG is also indicated for measles prophylaxis in individuals with PID who have been exposed to measles or who are at high risk of measles exposure.[1,4,5,8,9]

Hizentra, Cuvitru, Xembify, and Cutaquig are indicated as a subcutaneous (SC) infusion only.[4,7-9] Gammagard Liquid, Gammaked, and Gamunex-C may be administered as a SC infusion or an intravenous (IV) infusion for PID.[1-3] HyQvia is indicated for SC infusion only, with sequential infusion of the recombinant human hyaluronidase first and followed 10 minutes later with the immune globulin infusion.[5] The recombinant human hyaluronidase acts locally to increase dispersion and absorption of the immune globulin.

ANALYSIS OF EVIDENCE
The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage

Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of SCIG products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Cutaquig, Cuvitru, Gammagard Liquid, Gammaked, Gamunex-C, Hizentra, HyQvia, and Xembify is recommended in those who meet the following criteria:

FDA-Approved Indications

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1. Primary Immunodeficiencies. ^

Criteria. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):

i. Patient meets ONE of the following (a, b, or c):

Note: An exception can be made for the impaired antibody response if, according to the prescriber, the delay caused by pre-vaccination and post-vaccination antibody measurement would be deleterious to the patient's health. [IC-ISGP]

a) Patient has a diagnosis of congenital agammaglobulinemia, X-linked agammaglobulinemia, other agammaglobulinemia due to the absence of B-cells, Wiskott-Aldrich syndrome, ataxia telangiectasia, DiGeorge syndrome, severe combined immunodeficiency, Hyper-Immunoglobulin M (IgM) syndromes, an IgG level lower than 250 mg/dL, or a primary immune deficiency which has been confirmed by genetic or molecular testing; [IC-ISGP] OR

Note: Molecular testing is a type of genetic testing.

b) Patient has a diagnosis of common variable immunodeficiency, unspecified hypogammaglobulinemia, or other immunodeficiencies with significant hypogammaglobulinemia and meets the following [(1) and (2)]: [IC-ISGP]

(1) Patient's pretreatment IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); [IC-ISGP] AND

(2) Patient meets ONE of the following [(a) or (b)]:

(a) Patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); [IC-ISGP] OR

(b) Patient has recurrent infections; [IC-ISGP] OR

c) The patient has an IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency and meets the following [(1) and (2)]: [IC-ISGP]

(1) Patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); [IC-ISGP] AND

(2) Patient has recurrent infections; [IC-ISGP] AND

ii. The medication is prescribed by or in consultation with one of the following physician specialists: an allergist, immunologist, otolaryngologist (ear nose and throat [ENT] physician), pulmonologist, or an infectious diseases physician who treats patients with primary immune deficiencies. [IC-ISGP]

B) Patient is Currently Receiving Immune Globulin. Approve if the patient has been diagnosed with a primary immunodeficiency and according to the prescriber the patient is continuing to receive benefit from the product. [IC-ISGP]

Note: Examples of continued benefit with the product includes increased IgG levels or prevention and/or controlling of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, D, or E):

A) The patient is transitioning from immune globulin intravenous (IVIG), and the maintenance dose (given once weekly, every 2 weeks, or more frequently than once weekly [e.g., 2 to 7 times per week]) is based on the patient's previous monthly IVIG dose; OR
B) The patient is transitioning from another immune globulin subcutaneous (SCIG) product, and the maintenance dose (given once weekly, every 2 weeks, or more frequently than once weekly) is based on the patient's previous weekly SCIG dose; OR
C) The patient is initiating SCIG therapy without previous IVIG or SCIG therapy and is receiving a loading dose (e.g., 100 mg/kg once daily for 5 consecutive days) followed by once weekly (or more frequently as necessitated by volume) maintenance dosing; OR
D) The dose and interval between doses has been adjusted based on clinical response, as determined by the prescriber; OR
E) For a patient with primary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber; OR
F) For HyQvia only: Approve if the patient meets ONE of the following (i, ii, or iii):
- **i.** Patient is starting HyQvia and the dose and interval is being ramped-up to determine tolerability; OR
  Note: The patient may be switching from IVIG or from another SCIG product OR the patient may be naïve to immune globulin therapy. See prescribing information for ramp-up schedule.
- **ii.** Patient has already been started on HyQvia after the initial dose ramp-up and ONE of the following applies (a, b, or c):
  - **a)** The dose is 300 mg/kg to 600 mg/kg given at 3 to 4 week intervals; OR
  - **b)** The dose and frequency is the same as previously used when receiving IVIG; OR
  - **c)** The dose and interval between doses has been adjusted based on clinical response as determined by the prescriber.
- **iii.** For a patient with primary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber.

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2. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; [IC-L] AND
- **ii.** Electrodiagnostic studies support the diagnosis of CIDP; [IC-ISGP] AND
- **iii.** The medication has been prescribed by or in consultation with a neurologist. [IC-ISGP]

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a clinically significant improvement in neurological symptoms as determined by the prescriber. [IC-ISGP]
Note: Examples of improvement in neurologic symptoms include improvement in disability; nerve conduction study results improved or stabilized; physical examination show improvement in neurological symptoms, strength (e.g. grip strength), and sensation.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) The dose is either 0.2 g/kg or 0.4 g/kg per week administered in one or two sessions over 1 or 2 consecutive days; OR
B) The dose and interval between doses has been titrated and adjusted based on clinical response as determined by the prescriber; OR
C) For HyQvia only: Approve if the patient meets ONE of the following (i, ii, or iii):

i. Patient is starting HyQvia and the dose and interval is being ramped-up to determine tolerability; OR

ii. Patient has already been started on HyQvia after the initial dose ramp-up and ONE of the following applies (a, b, or c):

a) The dose and frequency is the same as the patient's previous IVIG treatment; OR

b) The dosing range is 0.4 g/kg to 2.4 g/kg, given in a frequency of 2-. 3-, or 4-week intervals; OR

c) The dose and interval between doses has been adjusted based on clinical response as determined by the prescriber; OR

iii. If the dose is ≤ 0.4 g/kg HyQvia may be administered without a ramp-up.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of immune globulin subcutaneous is not recommended in the following situations:

1. **Selective Immune Globulin A (IgA) Deficiency as the Sole Immunologic Abnormality.** Evidence does not support use of immune globulin.[15,24] Selective IgA deficiency is defined as a serum IgA level less than 0.07 g/L, but normal serum IgG and IgM levels in a patient greater than 4 years of age in whom other causes of hypogammaglobulinemia have been excluded.[24] Selective IgA deficiency may co-exist in some patients with poor specific IgG antibody production, with or without IgG2 subclass deficiency.[15,24] Some of these patients with a concomitant specific antibody defect might benefit from therapy with SCIG.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SOURCES OF INFORMATION

1. Gammagard® Liquid 10% [prescribing information]. Lexington, MA: Takeda; January 2024.
2. Gammaked™ 10% solution [prescribing information]. Fort Lee, NJ: Kedrion; January 2020.
3. Gamunex®-C 10% solution [prescribing information]. Research Triangle Park, NC: Grifols; January 2020.
4. Hizentra® 20% subcutaneous solution [prescribing information]. Kankakee, IL: CSL Behring; April 2023.
5. HyQvia® 10% subcutaneous solution with recombinant human hyaluronidase [prescribing information]. Lexington, MA: Takeda; January 2024.
6. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS; Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62:1-34.
7. Xembify® 20% subcutaneous solution [prescribing information]. Research Triangle Park, NC: Grifols; July 2024.
8. Cuvitru™ 20% subcutaneous solution [prescribing information]. Lexington, MA: Takeda; March 2023.
9. Cutaquig® 16.5% subcutaneous solution [prescribing information]. New York, NY: Pfizer; November 2021.
10. Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence. *J Allergy Clin Immunol.* 2017;139(3S):S1-S46.
11. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol.* 2015;136:1186-1205.
12. Centers for Medicare and Medicaid Services. Novitas Solutions, Inc. Local Coverage Determination (LCD): Immune Globulin (L35093) [Original effective date: 10/01/2015; Revision effective date: 2/5/2023]. Accessed on June 3, 2025.
13. Centers for Medicare and Medicaid Services. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Immune Globulin (A56786) [Original effective date: 10/03/2018; Revision effective date: 1/1/2025]. Accessed on June 3, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Policy created	New Medicare Advantage Medical Policy	08/02/2023

Policy revision	Removed drug specific criteria for HyQvia. HyQvia will use the same criteria as the other immune globulin products. **HyQvia dosing for Primary Immunodeficiencies**: The dose and interval between doses has been adjusted based on clinical response as determined by the prescribing physician was updated to prescriber. **HyQvia dosing for Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy** was added. Revision based on review of commercial policy revisions. Reviewed CMS surveillance – LCA revision, no changes based on LCA revision.	03/21/2024
Policy revision	**Primary Immunodeficiencies:** Added a note that molecular testing is a type of genetic testing. **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy:** Added grip strength as an example of an improvement at physical examination.	12/10/2024
Policy review	No criteria changes Based on LCD/LCA surveillance review	06/03/2025
Policy revision	No criteria changes. Formatting and notation updates.	06/17/2025

This policy was prepared and managed by CareContinuum and henceforth adopted by Blue Advantage effective 04/01/2026. Reviews are to be executed on behalf of Blue Advantage in accordance with applicable guidelines.