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) • Gammagard Liquid ERC® (immune globulin 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:	12/31/2025
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.[1-5,7-9,12] 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.[1,4,5,8,9,12]

Hizentra, Cuvitru, Xembify, and Cutaquig are indicated as a subcutaneous (SC) infusion only.[4,7-9] Gammagard Liquid, Gammaked, Gamunex-C, and Gammagard Liquid ERC may be administered as a SC infusion or an intravenous (IV) infusion for PID.[1-3,12] 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.

Immune globulin also is used for off-label indications. The National Comprehensive Cancer Network (NCCN) recommends specific SC dosing for immune globulin (100 to 200 mg/kg given SC weekly) for toxicities related to CAR-T and lymphocyte-engager related therapies.[13] The therapies themselves can result in secondary immunodeficiency.

- **B-cell chronic lymphocytic leukemia (CLL)**, is FDA-approved if given by the intravenous route.[14]
- **Hematologic neoplasm-associated hypogammaglobulinemia or hypogammaglobulinemia after B-cell targeted therapies (secondary immunodeficiency):** Immune globulin intravenous (IVIG) is used off-label for this indication.[13,15,16]
- **Hematopoietic cell transplantation (HCT) to prevent infections:** IVIG is used off-label for this indication.[17,18]
- **Multiple myeloma:** IVIG is used off-label for this indication.[13,19]

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 immune globulin subcutaneous products is recommended in those who meet one of 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.

Other Uses with Supportive Evidence

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3. B-Cell Chronic Lymphocytic Leukemia for Prevention of Infections. [@]

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 4 months if the patient meets BOTH of the following (i and ii):
- **i.** Patient meets ONE of the following (a or b):
  - **a)** Patient has an immunoglobulin G (IgG) level < 600 mg/dL (6.0 g/L); OR
  - **b)** Patient has a history of recurrent infections; AND
- **ii.** The medication is prescribed by or in consultation with an oncologist, hematologist, or infectious diseases physician; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a positive response to therapy, according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, D, E, F, or G):
A) The subcutaneous dose is 100 to 200 mg/kg given weekly; OR

B) 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
C) 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
D) 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
E) The dose and interval between doses have been adjusted based on clinical response, as determined by the prescriber; OR
F) 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
G) 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 are the same as previously used when receiving IVIG; OR
  - **c)** The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber; OR
- **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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4. Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia or treatment after B-cell Targeted Therapies (Secondary Immunodeficiency [SID]). @

Criteria. Approve for 6 months if the patient meets ONE of the following (A or B):
Note: Some examples of B-cell targeted therapy are chimeric antigen receptor (CAR)-T cell therapy (e.g., Kymriah [tisagenlecleucel intravenous infusion], Abecma [idecabtagene vicleucel intravenous infusion], Breyanzi [lisocabtagene maraleucel intravenous infusion], Tecartus [brexucabtagene autoleucel intravenous infusion], Yescarta [axicabtagene ciloleucel intravenous infusion]), a rituximab product, Besponsa (inotuzumab ozogamicin intravenous infusion), Blincyto (blinatumomab intravenous infusion).
Note: Refer to B-Cell Chronic Lymphocytic Leukemia (CLL) for Prevention of Infections and Multiple Myeloma for diagnosis-specific criteria.
A) Initial Therapy. Approve if the patient meets ONE of the following (i or ii):
- **i.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has an immunoglobulin G (IgG) level of < 600 mg/dL (6.0 g/L) [excluding paraprotein]; AND
  - **b)** Patient has recurrent or severe infections or there is a high risk of infection according to the prescriber; AND
  - **c)** The medication is being prescribed by or in consultation with an oncologist, hematologist, infectious disease physician, or immunologist; OR
- **ii.** Patient meets BOTH of the following (a and b):

a) Patient is < 18 years of age; AND
b) Patient will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy or other B-Cell targeted therapy; OR
Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion).
Note: Examples of other B-Cell targeted therapy includes: Besponsa (inotuzumab ozogamicin intravenous infusion), Blincyto (blinatumomab intravenous infusion).

B) Patient is Currently Receiving Immune Globulin. Approve if the patient is having a positive response to therapy, according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, D, E, F, or G):
A) The subcutaneous dose is 100 to 200 mg/kg given weekly; OR
B) 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
C) 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
D) 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
E) The dose and interval between doses have been adjusted based on clinical response, as determined by the prescriber; OR
F) For a patient with secondary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber; OR
G) 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 are the same as previously used when receiving IVIG; OR
c) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber; OR
iii. For a patient with secondary 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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5. Hematopoietic Cell Transplantation (HCT) to Prevent Infection. @

Criteria. Approve for the duration noted if the patient meets ONE of the following (A, B, or C):
A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient has had a HCT within the previous year; AND
ii. Patient has an immunoglobulin G (IgG) level < 600 mg/dL (6.0 g/L) OR the patient has multiple myeloma or malignant macroglobulinemia; AND

iii. According to the prescriber, the patient has a significant risk of having frequent and/or severe infections; AND
iv. The medication is prescribed by or in consultation with a hematologist, oncologist, or infectious diseases physician; OR

B) Initial Therapy. Approve for 3 months if the patient meets ONE of the following (i, ii, or iii):
i. Patient is a recipient of an umbilical cord blood transplant; OR
ii. Patient is undergoing transplantation for inherited or acquired disorders associated with B-cell deficiency; OR
iii. Patient with chronic graft versus host disease with recurrent sinopulmonary infections; OR

C) Patient is Currently Receiving Immune Globulin. Approve for 6 months if the patient is having a positive response to therapy according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level, controlling the number of infections, or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, D, E, F, or G):
A) The subcutaneous dose is 100 to 200 mg/kg given weekly; OR
B) 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
C) 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
D) 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
E) The dose and interval between doses have been adjusted based on clinical response, as determined by the prescriber; OR
F) For a patient with secondary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber; OR
G) 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 are the same as previously used when receiving IVIG; OR
c) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber; OR
iii. For a patient with secondary 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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6. Multiple Myeloma. @

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
i. Patient meets ONE of the following (a or b):

a) Patient has or is at risk of severe, recurrent infections according to the prescriber; OR
b) Patient will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy, or bispecific antibody therapy, or other B-Cell targeted therapy; AND

Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion).

Note: Examples of bispecific antibody therapy or other B-Cell targeted therapy includes: Elrexfio (elranatamab-bcmm subcutaneous injection), Tecvayli (teclistamab-cqyv subcutaneous injection), Talvey (talquetamab-tgvs subcutaneous injection).

ii. The medication is prescribed by or in consultation with a hematologist, oncologist, or infectious diseases specialist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year.

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

A) The subcutaneous dose is 100 to 200 mg/kg given weekly; OR
B) 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
C) 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
D) 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
E) The dose and interval between doses have been adjusted based on clinical response, as determined by the prescriber; OR
F) For a patient with secondary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber; OR
G) 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 are the same as previously used when receiving IVIG; OR
c) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber; OR

iii. For a patient with secondary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber.

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]. Cambridge, MA: Takeda; September 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]. Cambridge, MA: Takeda; July 2025.
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]. Cambridge, MA: Takeda; February 2025.
9. Cutaquig® 16.5% subcutaneous solution [prescribing information]. New York, NY: Pfizer; March 2025.
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. Gammagard Liquid ERC 10% intravenous or subcutaneous solution [prescribing information]. Cambridge, MA: Takeda; June 2025.
13. NCCN guidelines on the management of CAR-T cell and lymphocyte engager-related toxicities (version 2.2026 – November 11, 2025). ® 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 14, 2025.
14. Gammaked™ 10% solution [prescribing information]. Fort Lee, NJ: Kedrion; January 2020.
15. NCCN Drugs and Biologics Compendium. ® 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 14, 2025. Search term: Immune globulin.
16. Hayden PJ, Roddie C, Prader P, et al. Management of adults and children receiving CAR-T cell therapy. 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation and the Joint Accreditation Committee of ISCT and EBMT and the European Heaemtology Association. *Ann Oncol*. 2022;33:259-75.
17. Tomblyn M, Chiller T, Einsele H, et al; Center for International Blood and Marrow Research; National Marrow Donor program; European Blood and Marrow Transplant Group; American Society of Blood and Marrow Transplantation; Canadian Blood and Marrow Transplant Group; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America; Association of Medical Microbiology and Infectious Disease Canada; Centers for Disease Control and Prevention. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biol Blood Marrow Transplant.* 2009;1:1143-1238.
18. The NCCN guidelines on Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 3.2025 – September 24, 2025). © 2025 National Comprehensive Cancer Network. Available at : http://www.nccn.org. Accessed on November 10,2025.
19. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2026 – November 3, 2025). © 2025 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on November 10, 2025.
20. 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 December 15, 2025.
21. 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: 10/30/2025]. Accessed on December 15, 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
Policy review	No criteria changes Based on NCD/LCD/LCA surveillance review	10/24/2025
Policy revision	**Gammagard Liquid ERC was** added to the policy with the same criteria as all other immune globulin products. Criteria created for the following diagnoses: **B-Cell Chronic Lymphocytic Leukemia for Prevention of Infections, Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia or treatment after B-Cell Targeted Therapies (Secondary Immunodeficiency [SID]), Hematopoietic Cell Transplantation (HCT) to Prevent Infection,** and **Multiple Myeloma.**	12/31/2025

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.