

Subcutaneous Immune Globulins

(Cutaquig, Cuvitru, Gammagard Liquid, Gammagard Liquid ERC, Gammaked, Gamunex-C, Hizentra, HyQvia, Xembify)

When requesting Subcutaneous Immune Globulin (Cutaquig, Cuvitru, Gammagard Liquid, Gammagard Liquid ERC, Gammaked, Gamunex-C, Hizentra, Hyqvia, Xembify), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved off-label compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indications

Subcutaneous immune globulin (SCIG) injection is indicated for the treatment of:

- Primary humoral immunodeficiency including but not limited to, congenital agammaglobulinemia, common variable immunodeficiency, x-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.
- Chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.

Approved Off-label Compendial Uses

- B-cell chronic lymphocytic leukemia for prevention of infections
- Hematologic neoplasm-associated hypogammaglobulinemia or hypogammaglobulinemia or treatment after B-cell targeted therapies
- Hematopoietic cell transplantation to prevent infection
- Multiple myeloma

Coverage Guidelines

Primary Humoral Immunodeficiency

The individual must meet the following criteria for an initial authorization:

- Must have one of the following subtypes of primary immunodeficiencies:
 - o Common variable immunodeficiency (CVID);
 - o X-linked agammaglobulinemia;
 - o Congenital agammaglobulinemia;
 - o Other agammaglobulinemia due to absence of B-cells;
 - o Severe combined immunodeficiency (SCID);
 - o Wiskott-Aldrich syndrome;

- o Hyper-Immunoglobulin M (IgM) syndrome;
- o IgG level lower than 250 mg/dL;
- o DiGeorge syndrome;
- o Ataxia telangiectasis;
- o Other combined immunodeficiencies with significant hypogammaglobulinemia;
- o Unspecified hypogammaglobulinemia;
- o IgG subclass deficiency;
- o Selective antibody deficiency (SAD);
- o Other primary immune deficiency confirmed by genetic or molecular testing
- o
- For IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency, must have impaired antibody response (i.e., failure to produce antibodies to specific antigen); AND recurrent infections;
- For CVID, unspecified hypogammaglobulinemia, or other combined immunodeficiencies with significant hypogammaglobulinemia indications:
 - o The pretreatment total serum IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); AND
 - o Has an impaired antibody response (i.e., failure to produce antibodies to specific antigen) or has recurrent infections;
- The requested product is prescribed by or in consultation with one of the following physician specialists: allergist, immunologist, otolaryngologist (ear, nose, and throat [ENT] physician), pulmonologist, or an infectious disease physician who treats primary immune deficiencies.

Note: And exception can be made for the impaired antibody response if the delay caused by pre-vaccination and post-vaccination antibody measurement would be deleterious to the patient's health.

The Individual must meet the following criterion for reauthorization:

- Has been diagnosed with a primary immunodeficiency and is continuing to receive benefit from the product (e.g., increased IgG levels, preventing or controlling infections).

Approval duration (initial and renewal): 12 months

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The individual must meet all of the following criteria for an initial authorization:

- Is 18 years of age or older;
- The request product is prescribed by or in consultation with a neurologist;
- Electrodiagnostic studies support the diagnosis of CIDP.

The individual must meet the following criterion for reauthorization:

- Has a clinically significant improvement in neurological symptoms (e.g., improvement in disability; nerve conduction study results improved or stabilized; physical examination showing improvement in neurological symptoms, strength [e.g., grip strength], and sensation).

Approval duration (initial): 3 months

Approval duration (renewal): 12 months

B-Cell Chronic Lymphocytic Leukemia for Prevention of Infections

The individual must meet both of the following criteria for an initial authorization:

- Has an immunoglobulin G (IgG) level less than 600 mg/dL OR has a history of recurrent infections;
- The requested product is prescribed by or in consultation with an oncologist, hematologist, or infectious disease physician.

The individual must meet the following criterion for re-authorization:

- Is experiencing a positive response to therapy (e.g., maintaining an increased IgG trough level or a decrease in the number of infections).

Approval duration (initial): 4 months

Approval duration (renewal): 12 months

Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia after B-cell Targeted Therapies

NOTE: Examples of B-cell targeted therapy are chimeric antigen receptor (CAR) T cell therapy (e.g., Kymriah [tisagenlecleucel injection], Abecma [idecabtagene vicleucel injection], Breyanzi [lisocabtagene maraleucel injection], Tecartus [brexucabtagene autoleucel injection], Yescarta [axicabtagene ciloleucel injection]), a rituximab product, Besponsa (inotuzumab ozogamicin injection) and Blincyto (blinatumomab injection).

The individual must meet one of following criteria for an initial authorization:

- Meets all of the following:
 - o Has an immunoglobulin G (IgG) level less than 600 mg/dL;
 - o Has recurrent or severe infections or has high risk of infection;
 - o The requested product is prescribed by or in consultation with an oncologist, hematologist, infectious disease physician, or immunologist; OR
- Meets both of the following:
 - o Is less than 18 years of age; AND
 - o Will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy or other B-cell targeted therapy.

The individual must meet the following criterion for re-authorization:

- Is experiencing a positive response to therapy (e.g., maintaining an increased IgG trough level or a decrease in the number of infections).

Approval duration (initial and renewal): 6 months

Hematopoietic Cell Transplantation (HCT) to Prevent Infection

The individual must meet one of the following criteria for an initial authorization:

- Meets all of the following:
 - o Has had a HCT within the previous year;
 - o Has an immunoglobulin G (IgG) level less than 600 mg/dL OR has multiple myeloma or malignant macroglobulinemia;
 - o Has a significant risk of having frequent and/or severe infections;
 - o The requested product is prescribed by or in consultation with a hematologist, oncologist, or infectious disease physician; OR
- Is a recipient of an umbilical cord blood transplant; OR
- Is undergoing transplantation for inherited or acquired disorders associated with B-cell deficiency; OR
- Has chronic graft versus host disease with recurrent sinopulmonary infections.

The individual must meet the following criterion for re-authorization:

- Is experiencing a positive response to therapy (e.g., maintaining an increased IgG trough level, controlling the number of infections, or a decrease in the number of infections).

Approval duration (initial): 3 months

Approval duration (renewal): 6 months

Multiple Myeloma

The individual must meet the following criteria for an initial authorization:

- Meets one of the following:
 - o Has or is at risk of severe, recurrent infections; OR
 - o Will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy, biospecific antibody therapy, or other B-cell targeted therapy;
- The requested product is prescribed by or in consultation with a hematologist, oncologist, or infectious disease specialist.

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Dosing Recommendations

Cutaquig

Dosage for patients switching from IVIG

- Initial weekly dose = previous IVIG dose (in grams) x 1.40/No. of weeks between IVIG

Dosage for patients switching from SCIG:

- The weekly dose of Cuvitru is recommended to be the same as the weekly dose of prior SCIG treatment

Cuvitru

Dosage for patients switching from IVIG or Hyqvia:

- Initial weekly dose = previous IVIG or Hyqvia dose (in grams)/No. of weeks between IVIG or Hyqvia doses x 1.30
- Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week
- Biweekly dosing: multiply the calculated weekly dose by 2

Dosage for patients switching from SCIG:

- The weekly dose of Cuvitru is recommended to be the same as the weekly dose of prior SCIG treatment
- Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week
- Biweekly dosing: multiply the calculated weekly dose by 2

Gammagard Liquid/Gammaked/Gamunex-C

Primary immunodeficiency:

- The recommended dose is 1.37 x previous intravenous dose in grams divided by number of weeks between intravenous doses.

Hyqvia

Primary immunodeficiency:

Initial treatment interval/dosage ramp-up schedule:

- For patients previously on another immune globulin treatment, administer the first dose approximately one week after the last infusion of their previous treatment
- Increase the dose and frequency from a 1-week dose to a 3- or 4-week dose (see table below)

Week	Infusion Number	Dose Interval	Example for 30 grams per 4 weeks
1	1 st infusion	1-week-dose	7.5 grams
2	2 nd infusion	2-week-dose	15 grams
3	No infusion		
4	3 rd infusion	3-week-dose	22.5 grams
5	No infusion		
6	No infusion		
7	4 th infusion (if required)	4-week-dose	30 grams

Dosage for patients switching from IVIG:

- Administer Hyqvia at the same dose and frequency as the previous intravenous treatment, after the initial dose ramp-up

Dosage for patient naïve to SCIG treatment or switching from another SCIG:

- Administer Hyqvia at 300 mg/kg to 600 mg/kg at 3 to 4-week intervals, after initial ramp-up

Dosage for continuation of Hyqvia

- Administer Hyqvia at 300 mg/kg to 600 mg/kg at 3 to 4-week intervals
- Dose and interval between doses may be adjusted based on clinical response as determined by the prescriber
- The dose and frequency can be the same as previous IVIG dose

Chronic inflammatory demyelinating polyneuropathy (CIDP):

Dosage for patients switching from IVIG:

- Administer Hyqvia at the same dose and frequency as the previous intravenous treatment
- Dose and interval between doses may be ramped up to determine tolerability
- If the dose is ≤ 0.4 g/kg, Hyqvia may be administered without a ramp-up

Dosage for continuation of Hyqvia

- The dosing range is 0.4 g/kg to 2.4 g/kg, given in a frequency of 2 to 4-week intervals.
- Dose and interval between doses may be adjusted based on clinical response as determined by prescriber

Hizentra

Primary immunodeficiency:

- Hizentra can be administered at regular intervals from daily up to every 2 weeks
- For weekly or frequent dosing, start Hizentra 1 week after the last IVIG infusion or SCIG infusion
- For biweekly dosing, start Hizentra 1 or 2 weeks after the last IVIG infusion or 1 week after the last weekly SCIG infusion

Dosage for patients switching to Hizentra from IVIG:

- For weekly dosing: start Hizentra 1 week after last IVIG infusion
Initial weekly dose = previous IVIG dose (in grams)/No. of weeks between IVIG doses x 1.37
- For biweekly dosing: Multiply the calculated Hizentra weekly dose by 2
- For frequent dosing (2 to 7 times per week): Divide the calculated weekly dose by the desired number of times per week

Dosage for patients switching to Hizentra from SCIG:

- The previous weekly SCIG dose should be maintained

- For biweekly dosing: Multiply the previous weekly dose by 2
- For frequent dosing (2 to 7 times per week): Divide the previous weekly dose by the desired number of times per week.

Chronic inflammatory demyelinating polyneuropathy (CIDP):

- Initiate Hizentra 1 week after the last IVIG infusion.
- The recommended dose is 0.2 g/kg (1 mL/kg) per week. In the clinical study, a dose of 0.4 g/kg (2 mL/kg) per week was also safe and effective to prevent CIDP relapse.

Xembify

Dosage for treatment-naïve patients:

- The recommended dose is loading doses of 150 mg/kg/day for 5 consecutive days, followed by weekly administration starting at Day 8 at 150 mg/kg/week.

Dosage for patients switching to Xembify from IVIG:

- Initial weekly dose (grams) = prior IVIG dose (in grams) x 1.37/No. 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

Dosage for patients switching to Xembify from SCIG:

- Weekly dose (grams) should be the same as the weekly dose of prior SCIG treatment (grams)

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