

Subcutaneous Immune Globulins (Cutaquig, Cuvitru, Hizentra, Hyqvia, Xembify)



When requesting Subcutaneous Immune Globulin (Cutaquig, Cuvitru, Hizentra, Hyqvia, Xembify), the individual requiring treatment must be diagnosed with an FDA-approved indication 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.

Coverage Guidelines

Primary humoral immunodeficiency

Must have one of the following subtypes of primary immunodeficiencies:

- Common variable immunodeficiency (CVID)
- X-linked agammaglobulinemia
- Congenital agammaglobulinemia
- Other agammaglobulinemia due to absence of B-cells
- Severe combined immunodeficiency (SCID)
- Wiskott-Aldrich syndrome
- Hyper-Immunoglobulin M (IgM) syndrome
- IgG level lower than 250 mg/dL
- DiGeorge syndrome
- Ataxia telangiectasis,
- Other combined immunodeficiencies with significant hypogammaglobulinemia
- Unspecified hypogammaglobulinemia
- IgG subclass deficiency
- Selective antibody deficiency (SAD)
- Other primary immune deficiency confirmed by genetic or molecular testing

For an initial authorization request:

- Is 18 years of age or older (for Hyqvia only)
- The requested product is prescribed by or in consultation with one of the following physician specialist who treats patients with PID: allergist, immunologist, otolaryngologist (ear, nose, and throat [ENT] physician), pulmonologist, or infectious disease physician
- For IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency:
 - o The patient has impaired antibody response (i.e., failure to produce antibodies to specific antigen); AND
 - o The patient has recurrent infections
- For CVID, unspecified hypogammaglobulinemia, or other combined immunodeficiencies with significant hypogammaglobulinemia indications:
 - o The total serum IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); AND
 - o The patient has impaired antibody response (i.e., failure to produce antibodies to specific antigen); OR
 - o The patient has recurrent infections

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.

For re-authorization request:

- The patient is diagnosed with a primary immunodeficiency and is continuing to receive benefit from the product (e.g., increased IgG levels, preventing or controlling infections)
- Is 18 years of age or older (for Hyqvia only)

Chronic inflammatory demyelinating polyneuropathy (excludes Hyqvia):*For an initial authorization request:*

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

For a re-authorization request:

- Must have 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, and sensation)

Approval duration (initial and 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

Hyqvia

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 to 600 mg/kg at 3 to 4 week interval, after initial ramp-up

Hizentra**For 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 previously 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.

For 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 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 or prior SCIG treatment (grams)

References

1. Gammagard Liquid 10% [prescribing information]. Lexington, MA: Baxalta US; March 2021.
2. Gammaked™ 10% injection [prescribing information]. Fort Lee, NJ: Kedrion Biopharma, Inc.; January 2020.
3. Gamunex®-C 10% liquid [prescribing information]. Research Triangle Park, NC: Grifols USA, LLC; January 2020.
4. Hizentra® for subcutaneous infusion [prescribing information]. Kankakee, IL: CSL Behring LLC; April 2022.
5. HyQvia immune globulin infusion 10% with recombinant human hyaluronidase [prescribing information]. Lexington, MA: Baxalta US Inc.; March 2021.
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% solution [prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; August 2020.
8. Cuvitru subcutaneous 20% solution [prescribing information]. Westlake Village, CA: Baxalta US Inc.; March 2021.
9. Cutaquig 16.5% solution [prescribing information]. Hoboken, NJ: Octapharma USA, Inc.; July 2020.
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. Available at: [http://www.jacionline.org/article/S0091-6749\(16\)31141-1/pdf](http://www.jacionline.org/article/S0091-6749(16)31141-1/pdf). Accessed on August 9, 2021.
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. Immune globulin. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. [Updated; June 16, 2021; Accessed June 30, 2021].