# PRIOR AUTHORIZATION POLICY

**POLICY:** Immune Globulin Subcutaneous Prior Authorization Policy

- Cutaquig® (immune globulin subcutaneous 16.5% solution – Octapharma)
- Cuvitru™ (immune globulin subcutaneous 20% solution – Baxalta)
- Gammagard Liquid (immune globulin infusion 10% solution – Baxalta)
- 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)
- Xembify® (immune globulin subcutaneous 20% solution – Grifols)

**REVIEW DATE:** 10/12/2022

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## OVERVIEW

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.[4]
- **Primary humoral immune deficiency (PID),** for replacement therapy, including but is 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 (SCID).[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.[2-4,6,9]

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 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. HyQvia has a Limitation of Use that the safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than PID. The safety of HyQvia has also not been established in children.[5]

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of SCIG products. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with SCIG as well as the monitoring required for adverse events and long-term efficacy, initial approval requires SCIG products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation**: None.

**RECOMMENDED AUTHORIZATION CRITERIA**

**I.** Coverage of Cutaquig, Cuvitru, Gammagard Liquid, Gammaked, Gamunex-C, Hizentra, and Xembify (all listed products except HyQvia) is recommended in those who meet the following criteria:

**FDA-Approved Indications**

**1. Primary Immunodeficiencies.** 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.

**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; OR

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

**(1)** Patient's pretreatment IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); 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); OR

**(b)** Patient has recurrent infections; OR

**c)** Patient has an IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency and meets the following (1 and 2):

**(1)** Patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); AND

**(2)** Patient has recurrent infections; 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.

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

**2. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy.** Approve for the duration noted if the patient meets ONE 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.** The patient is ≥ 18 years of age; AND

**ii.** Electrodiagnostic studies support the diagnosis of CIDP; AND

**iii.** The medication has been prescribed by or in consultation with a neurologist; AND

**B)** Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a clinically significant improvement in neurologic symptoms, as determined by the prescriber.
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, and sensation.

**II.** Coverage of HyQvia is recommended in those who meet the following criteria:

**FDA-Approved Indications**

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

**A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):

**i.** Patient is ≥ 18 years of age; AND

**ii.** 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.

**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; OR

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

**(1)** Patient's pretreatment IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); 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); OR

**(b)** Patient has recurrent infections; OR

**c)** Patient has an IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency and meets the following (1 and 2):

**(1)** Patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); AND

**(2)** Patient has recurrent infections; AND

**iii.** 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.

**B)** Patient is Currently Receiving Immune Globulin. Approve if the patient meets BOTH of the following (i and ii):

**i.** Patient is ≥ 18 years of age; AND

**ii.** Patient has been diagnosed with a primary immunodeficiency and, according to the prescriber, is continuing to receive benefit from the product.
Note: Example of receiving benefit with the product includes increased IgG levels or, prevention and/or controlling of infections.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of SCIG 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 > 4 years of age in whom other causes of hypogammaglobulinemia have been excluded.[11] Selective IgA deficiency may co-exist in some patients with poor specific IgG antibody production, with or without IgG2 subclass deficiency.[10,11] Some of these patients with a concomitant specific antibody defect may 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.

## REFERENCES

1. Gammagard Liquid 10% [prescribing information]. Lexington, MA: Baxalta; March 2021.
2. Gammaked 10% injection [prescribing information]. Fort Lee, NJ: Kedrion Biopharma; January 2020.
3. Gamunex®-C 10% liquid [prescribing information]. Research Triangle Park, NC: Grifols; January 2020
4. Hizentra® for subcutaneous infusion [prescribing information]. Kankakee, IL: CSL Behring; April 2022.
5. HyQvia immune globulin infusion 10% with recombinant human hyaluronidase [prescribing information]. Lexington, MA: Baxalta; 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: August 2020.
8. Cuvitru™ subcutaneous 20% solution [prescribing information]. Lexington, MA: Baxalta; September 2021.
9. Cutaquig 16.5% solution [prescribing information]. Paramus, NJ: Octapharma; 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.