Reference number(s)
2043-A

SPECIALTY GUIDELINE MANAGEMENT

Subcutaneous Immune Globulin (SCIG): Hizentra®, HyQvia® and Cuvitru™

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. **Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)**
Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age and older.

B. **Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)**
1. Hizentra is indicated for the treatment of primary immunodeficiency in adults and pediatric patients 2 years of age and older.

2. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.

   Limitations of Use:
   Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.

C. **HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)**
HyQvia is indicated for the treatment of primary immunodeficiency in adults.

Limitation of use: Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review (for primary immunodeficiency only):

A. Diagnostic test results (when applicable)
1. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
2. Vaccine response to pneumococcal polysaccharide vaccine (post- vaccination *Streptococcus pneumoniae* antibody titers)

3. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
4. Pertinent genetic or molecular testing in members with a known genetic disorder

B. IgG trough level for those continuing with SCIG therapy

III. CRITERIA FOR INITIAL APPROVAL

A. Primary Immunodeficiency

Initial authorization of 12 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia):
   a. Diagnosis confirmed by genetic or molecular testing, or
   b. Pretreatment IgG level < 200 mg/dL, or
   c. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
   a. Diagnosis confirmed by genetic or molecular testing (if applicable), and
   b. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
   c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)
3. Common variable immunodeficiency (CVID):
   a. Age 4 years or older
   b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
   c. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age
   d. History of recurrent bacterial infections
   e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)
4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
   a. History of recurrent bacterial infections
   b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix)
   c. Any of the following pre-treatment laboratory findings:
      i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
      ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
      iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
      iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
      v. Specific antibody deficiency: normal IgG, IgA and IgM levels
5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.

B. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Hizentra only)

Initial authorization of 3 months may be granted for the maintenance treatment of CIDP in members currently receiving intravenous immune globulin (IVIG) therapy.

IV. CONTINUATION OF THERAPY

The following criteria apply to members who are currently receiving SCIG therapy through a paid pharmacy or medical benefit. All other members (including new members) must meet initial authorization criteria.

A. Primary Immunodeficiency

Authorization of 24 months may be granted when the following criteria are met:

1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of SCIG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of SCIG and consider a dose adjustment (when appropriate).

B. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Hizentra only)

Authorization of 24 months may be granted when the following criteria are met:

1. Maintenance of response from previous IVIG therapy
2. SCIG is being used at the lowest effective dose

V. APPENDIX

Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine:

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

VI. REFERENCES

1. Cuvitru [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2016.
2. Hizentra [package insert]. Kankakee, IL: CSL Behring LLC; October 2016.
3. HyQvia [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; February 2016.
4. Picard C, Al-Herz W, Bousfiha A, et al. Primary immunodeficiency diseases: an update on the classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency. *J Clin Immunol*. 2015; 35(8):696-726.
5. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015;136(5):1186-205.e1-78.
6. Orange JS, Ballow M, Stiehm ER, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: a working group report of the Basic and Clinical Immunology Interest section of the American Academy of Allergy, Asthma and Immunology. *J Allergy Clin Immunol*. 2012;130:S1-S24.
7. Ameratunga R, Woon ST, Gillis D, Koopmans W, Steele R. New diagnostic criteria for common variable immune deficiency (CVID), which may assist with decisions to treat with intravenous or subcutaneous immunoglobulin. Clin Exp Immunol. 2013;174(2):203-11.
8. Immune Deficiency Foundation. About primary immunodeficiencies. Specific disease types. http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/. Accessed Jun 12, 2017.
9. European Society for Immunodeficiencies. Diagnostic criteria for PID. http://esid.org/Working-Parties/Clinical/Resources/Diagnostic-criteria-for-PID2. Accessed July 8, 2016.

10. Immune Deficiency Foundation. *Diagnostic and Clinical Care Guidelines for Primary Immunodeficiency Diseases*. 3rd edition. Towson, MD: Immune Deficiency Foundation; 2015. http://primaryimmune.org/wp-content/uploads/2015/03/2015-Diagnostic-and-Clinical-Care-Guidelines-for-PI.pdf. Accessed June 12, 2017.
11. Shearer WT, Dunn E, Notarangelo LD, et al. Establishing diagnostic criteria for severe combined immunodeficiency disease (SCID), leaky SCID, and Omenn syndrome: the Primary Immune Deficiency Treatment Consortium experience. *J Allergy Clin Immunol.* 2014;133(4):1092.