SCIG Immune Globulin (subcutaneous immunoglobulin)

Description

SCIG Immune Globulin – Cutaquig, Cuvitru, Hizentra, Hyqvia, Xembify

Background

Human immune globulin therapy is used for the treatment of immunodeficiency, prophylaxis of infectious diseases, and in the management of a variety of other inflammatory and autoimmune disorders. There are two main routes of administration: intravenous (IV) and subcutaneous (SC). A third route is intramuscular (IM), although this is uncommonly used, except for hyper-immune globulins (eg, rabies immune globulin). There are also three different methods of administering immune globulin subcutaneously: traditional, facilitated subcutaneous, and subcutaneous rapid-push. Immune globulin products from human plasma were first used in 1952 to treat immune deficiency. Subcutaneous immunoglobulin (SCIG) contains the pooled immunoglobulin G (IgG) immunoglobulins from the plasma of approximately a thousand or more blood donors (1).

Regulatory Status

FDA-approved indications:
Cuvitru, Hizentra, and Xembify are indicated as replacement therapies for primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age and older. This includes, but is not limited to, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (2-4).

Hizentra is indicated for maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (3).
Cutaquig and Hyqvia are indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults. This includes, but is not limited to, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (5-6).

**Limitation of Use:**
Safety and efficacy of chronic use of recombinant human hyaluronidase in Hyqvia have not been established in conditions other than PI (5).

Immune globulin use is associated with increased risk of thrombosis, particularly in the elderly and patients with risk factors such as cardiovascular disease, hypercoagulopathy, those on estrogen therapy, and patients with central venous catheters. Patients should be monitored carefully for signs and symptoms of thrombosis (2-6).

IVIG products have been associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, > 65 years of age, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs (2-6).

Other potential complications to monitor include the following: (2-6)

**Immunoglobulin A deficiency:** People with this condition have the potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA.

**Aseptic meningitis syndrome (AMS):** Rare occurrences of AMS have been reported in association with IVIG treatment. AMS usually begins within several hours to 2 days following IVIG treatment and is characterized by symptoms including severe headache, drowsiness, fever, photophobia, painful eye movements, muscle rigidity, nausea, and vomiting. AMS may occur more frequently in association with high-dose (2 g/kg) IVIG treatment. Discontinuation of IVIG treatment has resulted in remission of AMS within several days without sequelae.

**Bleeding complications:** Bleeding complications may be encountered in patients with thrombocytopenia or other bleeding disorders.

**Severe reactions:** Severe reactions, such as anaphylaxis or angioneurotic edema, have been reported in association with IV immunoglobulins, even in patients not known to be sensitive to human immunoglobulins or blood products.

**Related policies**
Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

SCIG may be considered medically necessary for treatment of the following conditions: Primary Immunodeficiency Disease (PID) including, but not limited to: hypogammaglobulinemia, agammaglobulinemia, SCID (severe combined immunodeficiency disease), Wiskott-Aldrich syndrome, and CVID (common variable Immunodeficiency disease) and if the conditions indicated below are met.

Hizentra may be considered medically necessary for the treatment of CIDP (chronic inflammatory demyelinating polyneuropathy) and when the conditions below are met.

SCIG may be considered investigational for all other indications.

Prior-Approval Requirements

Age Cuvitru, Hizentra, and Xembify 2 years and older
Cutaquig and Hyqvia 18 years and older

Diagnoses

Patient must have ONE of the following:

1. Primary Immunodeficiency Disease (PID) with ONE of the following:
   a. Hypogammaglobulinemia, IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency with ALL of the following:
      i. Documented history of recurrent bacterial and viral infections
      ii. Impaired antibody response to pneumococcal vaccine
      iii. ONE of the following pre-treatment laboratory findings:
         1) Hypogammaglobulinemia: IgG < 500 mg/dL or > 2 SD below the mean age
         2) Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
         3) Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG
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<th>Section:</th>
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<th>Effective Date:</th>
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<td>Biologicals</td>
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and IgA levels
4) IgG subclass deficiency: IgG1, IgG2, or IgG3 > 2 SD below the mean age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
5) Specific antibody deficiency: normal IgG, IgA and IgM levels

b. SCID (severe combined immunodeficiency disease) or Agammaglobulinemia with **ONE** of the following
   i. Confirmed diagnosis by genetic or molecular testing
   ii. Pretreatment IgG level < 200 mg/dL
   iii. Absence or very low number of T cells (CD3 T cells < 300/microliter) or presence of maternal T cells in the circulation (SCID only)

c. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non SCID combined immunodeficiency) with **ALL** of the following:
   i. Confirmed diagnosis by genetic or molecular testing
   ii. Documented history of recurrent bacterial and viral infections
   iii. Impaired antibody response to pneumococcal vaccine

d. CVID (common variable Immunodeficiency disease) with **ALL** of the following:
   i. Documented history of recurrent bacterial and viral infections
   ii. Impaired antibody response to pneumococcal vaccine
   iii. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
   iv. Pretreatment IgG level < 500 mg/dL or > 2 SD below the mean for the age

Hizentra **ONLY**

2. Chronic inflammatory demyelinating polyneuropathy (CIDP)
   a. 18 years of age or older
   b. Previous treatment with immunoglobulin therapy (IVIG)
   c. Prescriber agrees to initiate Hizentra one week after the last infusion of IVIG
   d. Patient had significant improvement in disability and has maintained improvement while on previous immunoglobulin therapy (IVIG)

**AND ALL** of the following for **BOTH** indications:
a. Patients or caregivers have been instructed on how to monitor for signs and symptoms of thrombosis when self-administering the medication
b. NO dual therapy with other immune globulin medications

Prior – Approval Renewal Requirements

<table>
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<th>Age</th>
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<tr>
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<td>Cutaquig and Hyqvia</td>
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Diagnoses

Patient must have the **ONE** of following

1. Primary Immunodeficiency Disease (PID) with **ONE** of the following:
   a. Hypogammaglobulinemia, IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency
   b. SCID (severe combined immunodeficiency disease) or Agammaglobulinemia
   c. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non SCID combined immunodeficiency)
   d. CVID (common variable Immunodeficiency disease)

Hizentra **ONLY**

2. Chronic inflammatory demyelinating polyneuropathy (CIDP)
   a. 18 years of age and older
   b. CIDP symptoms have remained stable or improved since changing from previous immunoglobulin therapy (intravenous immunoglobulin)
   c. Chronic stable patients have been tapered and/or treatment withdrawn to determine whether continued treatment is necessary

**AND ALL** of the following for **BOTH** indications:

a. Reduction in frequency of bacterial and viral infections has been documented since initiation
b. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication)
c. The prescriber will re-evaluate the dose of the SCIG and reconsider a dose adjustment
d. Patients or caregivers have been instructed on how to monitor for signs and symptoms of thrombosis when self-administering the medication
e. **NO** dual therapy with other immune globulin medications

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

**Duration** 12 months

**Prior – Approval **Rezewnul Limits**

Same as above

**Rationale**

**Summary**

Human immune globulin therapy is used for the treatment of immunodeficiency, prophylaxis of infectious diseases, and in the management of a variety of other inflammatory and autoimmune disorders. Immune globulin products from human plasma were first used in 1952 to treat immune deficiency. Subcutaneous immunoglobulin (SCIG) contains the pooled immunoglobulin G (IgG) immunoglobulins from the plasma of approximately a thousand or more blood donors (1-6).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use SCIG while maintaining optimal therapeutic outcomes.

**References**


Policy History

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<td>October 2016</td>
<td>Addition of Cuvitru to PA and the addition of Hyqvia and Hizentra to this PA</td>
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<td>December 2017</td>
<td>Annual editorial review and reference update</td>
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<td>April 2018</td>
<td>Addition of the diagnosis of CIDP to addition and continuation criteria for Hizentra only</td>
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<tr>
<td>June 2018</td>
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<td>November 2018</td>
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<tr>
<td>March 2019</td>
<td>Annual editorial review and reference update. Updated CVID requirements per SME</td>
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<tr>
<td>June 2019</td>
<td>Addition of Cutaquig</td>
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<tr>
<td>September 2019</td>
<td>Annual review. Added references for PID diagnostic criteria per SME</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.