SCIG Immune Globulin (subcutaneous immunoglobulin)

Description

SCIG Immune Globulin – Cuvitru, Hizentra, Hyqvia,

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 and Hizentra 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 (2-3).

Hyqvia is 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 (4).

Limitation of Use:
Safety and efficacy of chronic use of recombinant human hyaluronidase in Hyqvia have not been established in conditions other than PI (4).

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 (2-4).

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 (2-4).

Other potential complications to monitor include the following: (2-4)
**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**
Atgam, GamaSTAN, IVIG
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, CVID (common variable Immunodeficiency disease) with listed requirements below.

SCIG may be considered investigational for all other indications.

Prior-Approval Requirements

Age       Cuvitru and Hizentra  2 years and older
          Hyqvia                  18 years and older

Diagnoses

Patient must have 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 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 <200mg/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. Age 4 years and older
   ii. Documented history of recurrent bacterial and viral infections
   iii. Impaired antibody response to pneumococcal vaccine
   iv. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
   v. Pretreatment IgG level < 500mg/dL or > 2 SD below the mean for the age

AND **ONE** of the following:
   a. Patients or caregivers have been instructed on how to monitor for signs and symptoms of thrombosis when self-administering the medication

### Prior – Approval Renewal Requirements

<table>
<thead>
<tr>
<th>Age</th>
<th>Cuvitru and Hizentra</th>
<th>2 years and older</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hyqvia</td>
<td>18 years and older</td>
</tr>
</tbody>
</table>

### Diagnoses

Patient must have 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
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)
i. Age 4 years and older

AND ALL of the following:
  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

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 12 months

Rationale

Summary
IVIG is used to provide immediate passive immunity after suspected exposure to an organism for which no active immunization exists or if there is inadequate time to develop active immunization, and as replacement therapy for patients with antibody deficiencies. The passive immunity imparted by IVIG is capable of attenuating or preventing infectious diseases or deleterious reactions from toxins, mycoplasma, parasites, bacteria, and viruses (1-4).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use SCIG while maintaining optimal therapeutic outcomes.
Section: Prescription Drugs  Effective Date: January 1, 2017
Subsection: Biologicals  Original Policy Date: October 21, 2016
Subject: SCIG  Page: 6 of 6

References

Policy History
<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>October 2016</td>
<td>Addition of Cuvitru to PA and the addition of Hyqvia and Hizentra to this PA</td>
</tr>
<tr>
<td>December 2016</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2016 and is effective on January 1, 2017.

Deborah M. Smith, MD, MPH