Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO038

Description

Immunoglobulin G is a subcutaneously administered immunoglobulin product that supplies a broad spectrum of immunoglobulin g (IgG) antibodies to restore abnormally low immune globulin G levels in patients and help in preventing infections.

Length of Authorization

- Initial:
  - i. PANDAS/PANS: three months
  - ii. All other covered indications: six months
- Renewal:
  - i. PANDAS/PANS: three months
  - ii. All other covered indications: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
immunoglobulin g (Hizentra)	Primary humoral immunodeficiency (PID); Chronic inflammatory demyelinating polyneuropathy (CIDP)	20% subcutaneous solution	920 mL/28 days
		1 g/5 mL prefilled syringe	920 mL/28 days
		2 g/10 mL prefilled syringe	920 mL/28 days
		4 g/20 mL prefilled syringe	920 mL/28 days
		10 g/50mL prefilled syringe	920 mL/28 days
immunoglobulin g (Gamunex-C)	Primary humoral immunodeficiency (PID); Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)/ pediatric acute-onset neuropsychiatric syndrome (PANS)	10% Subcutaneous solution	PID: 960 mL/28 days PAN/PANDAS: 2g/kg/dose
immunoglobulin g (Gammaked)		10% Subcutaneous solution	PID: 960 mL/28 days PAN/PANDAS: 2g/kg/dose
immunoglobulin g (Gammagard liquid)		10% Subcutaneous solution	PID: 690 mL/28 days PAN/PANDAS: 2g/kg/dose

immunoglobulin g (HyQvia)	Primary humoral immunodeficiency (PID)	10% Subcutaneous solution	700 mL/28 days
immunoglobulin g (Cuvitru)		20% Subcutaneous solution	460 mL/28 days
immunoglobulin g (Cutaquig)		16.5% Subcutaneous solution	576 mL/28 days

Initial Evaluation

I. **Immunoglobulin G** may be considered medically necessary when the following criteria below are met:
   A. A diagnosis of one of the following:
      1. **Primary immunodeficiency (PID)/Wiskott-Aldrich syndrome** (including but not limited to x-linked agammaglobulinemia, common variable immunodeficiency, transient hypogammaglobulinemia of infancy, IgG subclass deficiency with or without IgA deficiency, antibody deficiency with near normal immunoglobulin levels) and combined deficiencies (severe combined immunodeficiencies, ataxia-telangiectasia, x-linked lymphoproliferative syndrome)); **AND**
         i. For Hyqvia and Cutaquig: Patient must be ≥ 18 years old; **OR**
         ii. All other agents (Hizentra, Gamunex-C, Gammaked, Gammagard, Cuvitru); no age restriction; **AND**
         iii. Patient's IgG level is <200 mg/dL; **OR**
         iv. All of the following:
            a. Patient has a history of multiple hard to treat infections as indicated by at least one of the following:
               i. Four or more ear infections within 1 year
               ii. Two or more serious sinus infections within 1 year
               iii. Two or more months of antibiotics with little effect
               iv. Two or more pneumonias within 1 year
               v. Recurrent or deep skin abscesses
               vi. Need for intravenous antibiotics to clear infections
               vii. Two or more deep-seated infections including septicemia; **AND**
            b. The patient has a deficiency in producing antibodies in response to vaccination; **AND**
               i. Titers were drawn before challenging with vaccination; **AND**
               ii. Titers were drawn between 4 and 8 weeks of vaccination
      2. **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**; **AND**

i. Request is for Hizentra only; **AND**
ii. Patient must be ≥ 18 years old; **AND**
iii. Physician has assessed baseline disease severity utilizing an objective measure/tool (i.e slowing of nerve conduction velocity on electromyogram (EMG)/nerve conduction study (NCS); **AND**
   a. Used as initial maintenance therapy for prevention of disease relapses after treatment and stabilization with intravenous immunoglobulin (IVIG); **OR**
   b. Used for re-initiation of maintenance therapy after experiencing a relapse and requiring re-induction therapy with IVIG (see renewal for criteria)

3. **Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS); AND**
   i. Request is for Gammagard Liquid, Gammaked, or Gamunex-C only; **AND**
   ii. A consultation with a recommendation from a pediatric subspecialist (e.g., neurologist, pediatric psychiatrist, neurodevelopment pediatrician, rheumatologist, pediatric allergist/immunologist) as well as the recommendation of the patient's primary care provider (e.g., family physician, pediatrician, pediatric nurse practitioner, naturopath). The subspecialist consultation may be a teleconsultation. For adolescents, an adult subspecialist consult may replace a pediatric subspecialist consult; **AND**
   iii. A clinically appropriate trial of TWO or more less-intensive treatments (e.g., NSAIDs, corticosteroids, SSRIs, behavioral therapy, short-course antibiotic therapy) were either not effective, not tolerated, or did not result in sustained improvement in symptoms (as measured by a lack of clinically meaningful improvement on validated instrument directed at the patient's primary symptom complex). These trials may be done concurrently

II. Immunoglobulin g is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:
   A. Myasthenia gravis
   B. Postural Tachycardia Syndrome (POTS)
   C. Neuropathy

Renewal Evaluation

I. Renewal based on the following criteria:
   A. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity/anaphylaxis, thrombosis, aseptic meningitis syndrome, hemolytic anemia, hyperproteinemia, acute lung injury, etc.; **AND**
   B. For the following indications:
      1. **Primary immunodeficiency (PID)/Wiskott-Aldrich syndrome; AND**
         i. Disease response as evidenced by one or more of the following:
            a. Decrease in the frequency of infection
            b. Decrease in the severity of infection
      2. **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP); AND**
         i. Renewals will be authorized for patients that have demonstrated a beneficial clinical response to maintenance therapy, without relapses, based on an objective clinical measuring tool (i.e slowing of nerve conduction velocity on electromyogram (EMG)/nerve conduction study (NCS); **OR**
         ii. Patient is re-initiating maintenance therapy after experiencing a relapse while on Hizentra; **AND**
            a. Patient improved and stabilized on IVIG treatment; **AND**
            b. Patient was NOT receiving maximum dosing of Hizentra prior to relapse
      3. **Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS); AND**
         i. A reevaluation at three months by both the primary care provider and pediatric expert is required for continued therapy with IVIG. This evaluation must include clinical testing with a validated instrument, which must be performed pretreatment and posttreatment to demonstrate clinically meaningful improvement

Supporting Evidence

I. BUN and serum creatinine should be monitored in patients at risk for acute renal failure.
II. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy for an increased dosing frequency. Though a retrospective investigation has been done to evaluate an increased dosing frequency of Stelara retrospective review does not provide strong scientific evidence as do randomized controlled trials.

III. Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS):
- There are mixed results from two very small trials regarding the clinical effectiveness of IVIG for PANDAS. There is limited evidence to support the use of IVIG in PANS. IVIG has a significant rate of known harms.
- Expert opinion and lower-quality observational data indicate there may be benefit for some patients with these conditions, but recommended treatment protocols and criteria for treatment vary widely. Due to the severe impact of symptoms associated with PANDAS/PANS on child health, growth, and development, and the lack of known effective treatments, coverage of IVIG is recommended when recommended by the patient's PCP and a pediatric subspecialist, and after less-intensive therapies were not effective, were not tolerated, or did not result in sustained improvement in symptoms. The recommendation is weak because of the very low quality of the evidence.

Investigational or Not Medically Necessary Uses

I. Clinical trials are ongoing for the following indications:
   A. Myasthenia gravis
   B. Postural Tachycardia Syndrome (POTS)
   C. Neuropathy

References

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Policy Implementation/Update:

Action and Summary of Changes	Date
Added new 10 g/50mL prefilled syringe to policy	05/2023
Inclusion of PANS/PANDAS indications for IVIG products (Gammagard Liquid, Gammaked, and Gamunex-C) and supporting evidence at the guidance of the state of Oregon Health Evidence Review Commission (HERC).	03/2023
Addition of Hizentra syringe formulation	04/2020
Conversion to policy and addition of Cutaquig	06/2019
Updated criteria to include new indication for Hizentra in chronic inflammatory demyelinating polyneuropathy and added question to allow approval for Cuvitru in the setting of primary humoral immunodeficiency (PI).	04/2018
Previous reviews	03/2016, 02/2016
Criteria creation and implementation	02/2015