



## Prior Authorization Approval Criteria

### Intravenous immunoglobulin and subcutaneous immunoglobulin

**Generic name:** Intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG)

**Brand name:** Refer to table below for IVIG, Vivaglobulin® (SCIG) and Hizentra 20% (SCIG)

**Medication class:** Immune globulin

**FDA approved uses:**

- SCIG: treatment of primary immune deficiencies
- IVIG: please refer to the table below

(IVIG: By brand name and indications)

PID	ITP	BMT	CLL	KD	Pediatric HIV
Carimune NF Flebogamma 5% Gamimune N 10% Gammagard S/D Gammar –P IV Gamunex Iveegam EN Octagam 5% Panglobulin NF Polygam S/D	Carimune NF Gamimune N 10% Gammagard S/D Gamunex Panglobulin NF Polygam S/D	Gamimune N 10%	Gammagard S/D Polygam S/D	Gammagard S/D Iveegam EN Polygam S/D	Gamimune N 10%

PID: primary immune deficiencies

- congenital agammaglobulinemia (X-linked agammaglobulinemia)
- hypogammaglobulinemia
- common variable immunodeficiency\* (please see criteria for use in CVID following this section)
- X-linked immunodeficiency with hyperimmunoglobulin M
- severe combined immunodeficiency
- Wiskott-Aldrich syndrome

ITP: idiopathic thrombocytopenic purpura:

- Platelet counts must be less than  $30 \times 10^9/L$ .
- Corticosteroids are recommended as first line treatment, but if they are contraindicated in a patient then IVIG may be considered.
- IVIG may be used when a rapid response is required, in cases with life threatening bleeding complications or active mucocutaneous bleeding is present.
- Treatment is generally not indicated for platelet counts greater than  $50 \times 10^9/L$  when the following are absent: bleeding to platelet dysfunction, trauma, need for surgical correction, or clearly identified comorbidities for bleeding.

BMT: bone marrow transplant

CLL: chronic lymphocytic leukemia

KD: Kawasaki disease

Pediatric HIV: Pediatrics infected with HIV/AIDs, treatment or prevention.

**Off-label uses:**

Blood diseases:

- multiple myeloma and immunoproliferative neoplasms
- agranulocytosis
- autoimmune hemolytic anemia
- Post-transfusion purpura
- Neonatal alloimmune thrombocytopenia

Infectious diseases:

- Solid organ transplant recipients at risk for CMV and pneumonia.
- Parvovirus B19 infection chronic with severe anemia.

Neurologic diseases:

- Guillain Barre Syndrome (400mg/kg/day x 5 days)
- Chronic severe myasthenia gravis (400mg/kg/day ax 5 days)
- hereditary and idiopathic peripheral neuropathy
- idiopathic progressive polyneuropathy
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- multifocal motor neuropathy
- polymyositis
- Moersch-Woitmann syndrome (stiff man syndrome)
- Multiple sclerosis, relapsing remitting, when other therapies are insufficient.

Other:

- Hyper IGE syndrome
- dermatomyositis 2gm/kg/month x 3 months, then must re-assess
- autoimmune mucocutaneous blistering diseases; biopsy proven pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid and epidermolysis bullosa acquisita for patients who have failed conventional therapies or in whom conventional therapies are contraindicated, or in whom conventional therapies would not work fast enough.

**Available dosage forms:** Injection, solution and powder for reconstitution

**Usual dose:**

SCIG: Children  $\geq 2$  years and adults: 100-200 mg/kg subcutaneously weekly

- max rate: 20 mL/hour
- doses  $>15$  mL should be divided between sites
- *Treatment may be transitioned to the home/home care setting in the absence of adverse reactions*

Hizentra:

Children  $\geq 2$  years and adults: the dose should be individualized based on the patients clinical response to Hizentra therapy and serum immunoglobulin G (IgG) trough levels.

- max rate: 25 mL/hour/site
- *Treatment may be transitioned to the home/home care setting in the absence of adverse reactions*

IVIg: To be infused intravenously over 2-24 hours

- Pediatric HIV: 400 mg/kg every 28 days
- PID: 200-400 mg/kg every 4 weeks or as per monitored serum IgG concentrations
  - Gammagard® Liquid, Gamunex®, Octagam®: 300-600 mg/kg every 3-4 weeks
- CLL: 400 mg/kg/dose every 3 weeks
- ITP: Acute: 400 mg/kg/day for 5 days or 1000 mg/kg/day for 1-2 days  
Chronic: 400 mg/kg as needed to maintain platelet count  $>30,000/\text{mm}^3$ ; may increase dose to 800 mg/kg (1000 mg/kg if needed)
- KD: Initiate within 10 days of onset: 2 g/kg as a single dose over 10 hrs, or 400 mg/kg/day for 4 days. **Note:** Used in combination with aspirin: 80-100 mg/kg/day in 4 divided doses for 14 days; when fever subsides, dose aspirin at 3-5 mg/kg once daily for  $\geq 6$ -8 weeks
- BMT: 500 mg/kg beginning on days 7 and 2 pretransplant, then 500 mg/kg/week for 90 days post-transplant

Off-Label

- Refractory Polymyositis: 1 g/kg/day x 2 days every month x 4 doses
- Refractory Dermatomyositis: 2g/kg/dose every month x 3-4 doses
- Autoimmune Hemolytic Anemia and Neutropenia: 1000 mg/kg/dose for 2-3 days
- Guillain-Barre Syndrome: 400 mg/kg/day for 5 days
- CIDP: variable doses used
  - 400 mg/kg/day for 5 doses once each month
  - 800 mg/kg/day for 3 doses once each month

- 1000 mg/kg/day for 2 days once each month
- Myasthenia Gravis: 2 g/kg divided over 2 days

**Approximate yearly cost** (AWP 2010) If treating PID :

SCIG:

Hizentra: 228 mg/kg/week, \$124,104.00 (dose based on mean dose in clinical study)

Vivaglobin: 150 mg/kg/week, \$77,760.00 (dose based on mean dose in clinical study)

IVIG: 600 mg/kg/4 week, \$ 74,466.00 (based on Gammagard; dose range is 300-600 mg every 3-4 weeks)

*Note: All doses based on a weight of 75 kg.*

**Duration of therapy:** Varies for individual disease states (4 days to months) depending on clinical responses, trough IgG levels, and patient tolerability.

**Criteria for use** (bullet points below are all inclusive unless otherwise noted):

- The indicated diagnosis (including any applicable labs and /or tests) and medication usage must be supported by documentation from the patient's medical records.
- Clinically diagnosed with any of the above disease states listed under FDA approved and Off label uses.
- Risk/benefit assessment for patients with acute renal failure or those predisposed to acute renal failure (ie: DM, sepsis, paraproteinemia, etc), cardiovascular disease, or history of thrombotic events
- Patient does not have IgA deficiency or sensitization to IgA
- Patient has not received a live virus vaccine within 3 weeks prior to receiving IVIG.
- Medical services must meet nationally recognized standard for quality care and are provided at the appropriate level of care and place of service. The first dose may be given at the facility of choice by the physician, all subsequent doses will be given by home infusion. The following are some exceptions that may be acceptable for services outside the home:
  - Documented history of a severe reaction to IVIG or blood products. Severe reaction is defined as anaphylactic reaction. The patient should have a history of reactions and not be based on the potential of IVIG to induce such reactions.
  - Documented intolerance to IVIG requiring constant telemetry monitoring of vitals.
  - Unsafe home environment.
  - No access to 911 services.
  - Documented presence of IGA auto antibodies.
  - Patient is severely decompensated e.g. respiratory failure in a myasthenic crisis.

**Criteria for continuation of therapy:**

- $Cl_{cr} > 10$  mL/min
- Patient is tolerant to treatment regimen
- Re-evaluate treatment regimen after initial treatment in order to assess further need for continuation depending on clinical responses

**Cautions:**

- Anaphylactic reactions can occur, especially with IgA deficient patients
- Possibility of high risk of renal dysfunction: elderly, patients with renal disease, DM, volume depletion, sepsis, paraproteinemia
- Possibility transmission of infectious agents
- Patients should be appropriately hydrated prior to therapy

**Monitoring:** BUN, renal function, urine output, hemoglobin and hematocrit, infusion-related adverse reactions, anaphylaxis.

**Contraindications:** Hypersensitivity to immune globulin, selective IgA deficiency.

**Not approved if:**

- Above criteria are not met.

- Patient has hypersensitivity to immune globulin.
- Being prescribed for any of the following conditions:
  - acute lymphoblastic leukemia
  - aplastic anemia
  - Diamond-Blackfan anemia
  - non-immune thrombocytopenia
  - red cell aplasia
  - Behçets syndrome
  - inclusion body myositis
  - rheumatoid arthritis
  - scleroderma
  - systemic lupus erythematosus
  - Wegners granulomatosis, Goodpastures syndrome, polyarteritis nodosa, vasculitis associated with connective tissue diseases
  - chronic sinusitis
  - recurrent otitis media
  - asthma
  - chronic fatigue syndrome
  - cystic fibrosis
  - diabetes mellitus
  - hemolytic uremic syndrome
  - adrenoleukodystrophy
  - epilepsy
  - nephrotic syndrome
  - Von Willebrand's syndrome
  - other conditions not listed above

**Special considerations:**

- May impair responses to live virus vaccines; separate administration by at least 3 months
- Subcutaneous weekly treatments provide more constant levels rather than the more pronounced peak and trough patterns observed with I.V. monthly immune globulin treatments
- Conversion from I.V. to SubQ:
  - Multiply previous I.V. dose by 1.37(for Vivaglobin) or 1.53 (for Hizentra) then divide this dose into weekly doses based on the patient's previous IGIV treatment interval:

$$\text{Initial Vivaglobin or Hizentra dose} = \frac{1.37 \text{ or } 1.53 \times \text{previous IGIV dose (in grams)}}{\text{Number of weeks between IGIV doses}}$$

- Adjust the dose over time to achieve desired clinical response or target IgG levels
- SubQ infusion administration should begin 1 week after the last I.V. dose

P&T Approval: \_\_\_\_\_ Date: \_\_\_\_\_

Adopted: 11/16/04

Revised: 06/13/07, 09/08/10, 03/14/12