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Policy Number: 013.006 **Title: Coverage Determination Policy for Intravenous Immune Globulin (IVIG)**		

Regions: ☒ Texas ☐ Florida ☐ Indiana ☐ New Jersey ☒ New Mexico

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA:

- New Jersey, New Mexico & Texas, Local Coverage Determination (LCD): Intravenous Immune Globulin (IVIG) (L35093). Available at: L35093
- New Jersey, New Mexico & Texas, Local Coverage Article (LCA): Self-Administered Drug Exclusion List: (A52800). Available at: A52800
- National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3). Available at 250.3

Disclaimer:

WellMed Coverage Determination Policies are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support WellMed coverage decision making. WellMed may modify these Policy Guidelines at any time. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the WellMed Coverage Determination Policies is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Doctors helping patients for more than 25 years

Title: Coverage Determination Policy for Intravenous Immune Globulin (IVIG)

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Coverage Policy Number: 013.006

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Step Therapy Criteria

This policy supplements the Medicare guidelines such as NCDs, LCDs, and other Medicare manuals for the purposes of determining coverage under the Part B medical benefits. This Step Therapy Policy is implemented to enforce a step therapy requirement for new starts only. This policy is not applicable to members continuing therapy within the past 365 days. Coverage is granted if Medicare Coverage requirements PLUS these step criteria are met.

1. Subcutaneous Immune Globulin

Preferred drug(s): Cuvitru, Hizentra, HyQvia, Xembify

Non-preferred drug(s): Cutaquig

Non-Preferred Product Step Therapy Criteria

Cutaquig may be covered when **ANY** of the following are met:

A. History of use of any of the above-preferred drugs with a minimal clinical response

B. History of contraindication, intolerance or severe adverse event to all preferred drugs

C. Continuation of prior therapy within the past 365 days

2. Intravenous Immune Globulin

Preferred drug(s): Privigen, Bivigam, Gammaplex, Gamunex-C/Gammaked, Carimune NF/Gammagard S/D, Octagam, Gammagard liquid, Flebogamma DIF

Non-preferred drug(s): Panzyga, Asceniv

A. History of use of at least two of the above-preferred drugs with a minimal clinical response

B. History of contraindication, intolerance or severe adverse event to all preferred drugs

C. Continuation of prior therapy within the past 365 days

Coverage Determination

IVIG and SCIG may be covered under Part B if the criteria in the Medicare NCD and LCD are met.

1. WellMed will cover IVIG for the treatment of **Autoimmune Bullous diseases (pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane (cicatricial) pemphigoid, epidermolysis bullosa acquisita, pemphigoid gestationis and linear IgA bullous dermatosis)**
   A. Diagnosis of extensive and debilitating autoimmune bullous disease
   B. History of failure, contraindication, or intolerance to systemic corticosteroids in combination with immunosuppressive agents (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil)
   C. **I**VIG dose does not exceed 1,000 to 2,000 mg/kg per month divided into 3 equal doses, each given over 3 days OR 400 mg/kg per day given over 5 days per month
   D. For long term treatment, documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

2. WellMed will cover IVIG for use in **Idiopathic Thrombocytopenic Purpura (ITP)** when the following criteria are met:
   A. Diagnosis of acute ITP
   B. Documented platelet count of < 50 x 10^9 /L obtained within the past 30 days
   C. IVIG dose does not exceed 1000mg/kg/day for 1 to 2 days

   OR

   A. Diagnosis of chronic ITP
   B. History of failure, contraindication, or intolerance to at least **ONE** of the following:
      - Corticosteroids
      - Splenectomy
   C. Duration of illness of greater than 6 months
   D. No concurrent illness/disease explaining thrombocytopenia
   E. Platelet counts persistently at or below 20 x 10^9 /L
   F. IVIG dose does not exceed 2000mg/kg per month given over 2 to 5 consecutive days

3. WellMed will cover IVIG for use as replacement therapy in patients with diagnosis of **Primary Immunodeficiencies** when the following criteria are met:

   A. Clinically significant functional deficiency of humoral immunity as evidenced by **ONE** of the following:
      - Documented failure to produce antibodies to specific antigens
      - History of significant recurrent infections
   B. The initial IVIG dose is 200 to 800 mg/kg every 3 to 4 weeks based on product FDA-labeled dosing and should be titrated according to patient response
   C. Member has **ONE** of the primary Immunodeficiencies listed below:
      - Congenital Agammaglobulinemia
      - X-linked immunodeficiency with hyper-IgM
      - Common Variable Immunodeficiency (CVID)
      - Wiskott-Aldrich syndrome
      - Severe combined Immunodeficiencies
      - Deficient qualitative or quantitative antibody production
      - Have at least one bacterial infection directly attributable to this deficiency

4. WellMed will cover IVIG for the **prevention of infection in B-cell Chronic Lymphocytic Leukemia (CLL)** when **ALL** of the following criteria are met:

   A. Diagnosis of B-cell chronic lymphocytic leukemia
   B. Documented hypogammaglobulinemia (IgG < 600mg/dL)
   C. History of serious bacterial infection(s) associated with B-cell CLL requiring either oral or parenteral antibiotic therapy
   D. IVIG dose does not exceed 400 mg/kg every 3 to 4 weeks

5. WellMed will cover IVIG for **Multifocal Motor Neuropathy** when **ALL** of the following criteria are met:

INITIAL

A. IVIG may be considered for first line of treatment of patients who have progressive, symptomatic multifocal motor neuropathy that has been diagnosed on the basis of electrophysiology findings that rule out other possible conditions that may not respond to this treatment
B. Initial Dose: IV: 2 g/kg (administered in divided doses)

MAINTENANCE

A. With an objective benefit, the IVIG could continue at REDUCED dose, and progressive tapering

   **Maintenance Dose IV: Titrated to the lowest possible dose (less than initial dose) every 3 to 6 weeks (administered in divided doses)*

B. For long-term treatment of stable patients (> 1 year), the dose must be periodically reduced to the lowest possible dose or withdrawn, and the effects measured, in order to validate continued use
C. Maintenance therapy should be at the lowest possible dose of IVIG

6. WellMed will cover IVIG for **Warm-type Autoimmune Hemolytic Anemia** that is unresponsive to corticosteroids or splenectomy, unless contraindicated

7. WellMed will cover IVIG for **Severe Active Systemic Lupus Erythematosus** for whom other interventions have been unsuccessful, have become intolerable, or are contraindicated

8. WellMed will cover IVIG for **Scleromyxedema.** Medical records must be reviewed if therapy extends longer than 6 months to assess overall improvement and whether the provider is using the least amount of IVIG to maintain the positive changes

9. WellMed will cover IVIG for **Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN)** when the following are met:
   A. SCORTEN level of 3 or greater
   B. Prescribed as a one-time treatment only, subsequent RENEWAL requests will be denied

10. WellMed will cover IVIG for **Systemic Capillary Leak Syndrome (SCLS)** or **Clarkson's disease** when given monthly prophylactically and tapered to the lowest effective dose. All other claims will have the appeals process for potential coverage where medical documentation and submitted literature can be reviewed for individual consideration.

11. WellMed will cover IVIG for **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)** when **ALL** of the following criteria are met:

INITIAL

Diagnosis of **CIDP** a confirmed by:

A. Progressive symptoms present for at least 2 months; and
B. Symptomatic Polyradiculoneuropathy as indicated by progressive or relapsing motor or sensory impairment of more than one limb; and
C. Electrodiagnostic findings consistent with EFNS/PNS guidelines for definite CIDP indicating at least **ONE** of the following criteria:
   - Motor distal latency prolongation in 2 nerves
   - Reduction of motor conduction velocity in 2 nerves
   - Prolongation of F-wave latency in 2 nerves
   - Absence of F-waves in at least 1 nerve
   - Partial motor conduction block of at least 1 motor nerve
   - Abnormal temporal dispersion in at least 2 nerves
   - Distal CMAP duration increase in at least 1 nerve

MAINTENANCE

A. Patients responsive to an initial course of IVIG will be eligible for maintenance therapy coverage only if unequivocal neurological deterioration occurs at some future point in time.
B. If no significant improvement as outlined in the above guidelines, therapy should be discontinued.
C. Maintenance therapy should be at the lowest dose of IVIG possible.
D. Although patients will vary in response, after a one to two-year period of stable therapy, attempts to reduce should be occurring.

**Continued dosing without attempts to reduce the dosing and check responses would be considered inappropriate and subject to pre and post pay reviews.*

12. WellMed will cover IVIG for **Kawasaki disease** when **ALL** of the following criteria are met:
    A. Diagnosis of Kawasaki disease
    B. IVIG dose dose not exceed 400mg/kg for five consecutive days or a single dose of 2000mg/kg

13. WellMed will cover IVIG after **Allogeneic Bone Marrow Transplant** when **ALL** of the following criteria are met:
    A. Prevention of acute graft vs host disease (GVHD) or prevention of infection
    B. Confirmed allogeneic bone marrow transplant within the last 100 days
    C. Documented severe hypogammaglobunlinemia (IgG < 400 mg/dL)
    D. IVIG dose does not exceed 500mg/kg once weekly for the first 90 days of therapy, then monthly up to 360 days after transplantation

14. WellMed will cover IVIG for **Dermatomyositis** or **Polymyositis** when the following criteria are met:
    A. Diagnosis of Dermatomyositis or Polymyositis
    B. History of failure, contraindication or intolerance to immunosuppressive therapy (e.g, azathioprine, corticosteroids, cyclophosphamide, methotrexate)
    C. IVIG dose does not exceed 2,000 mg/kg per month given over 2 to 5 days

15. WellMed will cover IVIG for **Acute Relapse of Relapsing Remitting Multiple Sclerosis (RRMS)** when the following criteria are met:

INITIAL

A. Diagnosis or relapsing forms of multiple sclerosis (MS)
B. Documentation of an MS exacerbation or progression of the patient's clinical status as compared to their status prior to initiation of IVIG
C. History of failure, contraindication or intolerance to at least **TWO** of the following agents:
    - Aubagio (teriflunomide)
    - Avonex (interferon beta-1a)
    - Bafiertam (monomethyl fumarate)
    - Betaseron (interferon beta-1b)
    - Copaxone/Glatopa (glatiramer acetate)
    - Extavia (interferon beta-1b)
    - Gilenya (fingolimod)
    - Lemtrada (alemtuzumab)
    - Mavenclad (cladribine)
    - Mayzent (siponimod)
    - Ocrevus (ocrelizumab)
    - Plegridy (peginterferon beta-1a)
    - Rebif (interferon beta-1a)
    - Tecfidera (dimethyl fumarate)
    - Tysabri (natalizumab)
    - Vumerity (diroximel fumarate)
D. Induction dose does not exceed 400mg/kg/day for up to 5 days

CONTINUATION

A. Medical records, including findings of interval examination including neurological deficits incurred and assessment of disability [e.g., Expanded Disability Status Scale (EDSS), Functional Systems Score (FSS), Multiple Sclerosis Functional Composite (MSFC), Disease Steps (DS)]
B. Documentation of decreased number of relapses since starting immune globulin therapy
C. Quantitative assessment to monitor and document the progress is required which may include any accepted metric assessment such as activities of daily living (ADL) measurement. Changes in these measures must be clearly documented. Subjective or experiential improvement alone is insufficient to continue IVIG.
D. Diagnosis continues to be the relapsing forms of MS
E. Prescribed by or in consultation with a neurologist
F. IVIG dose does not exceed 1,000 mg/kg monthly
G. When improvement has occurred, attempts to decrease/wean the dosage must be made and documented. Following dosage reduction, if improvement is sustained, an attempt to discontinue IVIG must be made. If documentable improvement does not occur with IVIG administration, then infusions should not continue.
H. Periodically (at least every 3 months or less) attempt should be made to titrate to the lowest possible dose or wean off IVIG. If there are objective findings then patient could go back to last dose for no more than 3 months and then try taper again.

**For Example; if patient is on 2g/kg and weaned to 1 g/kg then to 0.5 g/kg and they had objective changes then they can return to 1 g/kg*

NOTE:

- *IVIG is generally not considered effective for maintenance therapy of MS or in slowing disease progression*
- *Symptoms such as numbness, fatigue, pains, spasms, brain fog or a feeling of generalized weakness are considered subjective symptoms and should not be considered in objective benefit evaluation or objective measures used to determine initial efficacy.*

16. WellMed will cover IVIG for **Myasthenia Gravis** when **ALL** of the following are met:

I. **Myasthenia exacerbation**
   A. Diagnosis of generalized myasthenia gravis
   B. Evidence of myasthenic exacerbation, defined by at least **ONE** of the following symptoms in the last month:
      - Difficulty swallowing
      - Acute respiratory failure
      - Major functional disability responsible for the discontinuation of physical activity
      - Recent immunotherapy treatment with a checkpoint inhibitor
   C. History of failure, contraindication, or intolerance to immunomodulator therapy or currently receiving immunomodulator therapy
   D. IVIG dose does not exceed 2,000 mg/kg per month given over 2 to 5 days administered in up to three monthly infusions

II. **Refractory Myasthenia Gravis**
   A. Diagnosis of refractory generalized myasthenia gravis
   B. Documentation that the disease status is unchanged or worsening (persistent or worsening symptoms that limit functioning) despite failure, contraindication, or intolerance to **BOTH** of the following (used in adequate doses and duration):
      - Corticosteroids
      - Two immunomodulator therapies (e.g., azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, tacrolimus)
   C. Currently receiving immunomodulator therapy used in adequate doses, for long-term management of myasthenia gravis
   D. IVIG dose does not exceed 2,000 mg/kg per month given over 2 to 5 days. Dosing interval may need to be adjusted in patients with severe comorbidities

NOTE: *For off-label indications not specifically mentioned above, please reference CMS Benefit Policy Manual Chapter 15; 50 Drugs and Biologicals, Section 4.5 Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen for criteria when relevant.*

17. WellMed will cover IVIG for **Stiff Person Syndrome (SPS)** when **ALL** of the following are met:

INITIAL

A. Diagnosis of Stiff Person Syndrome (SPS)
B. Symptom control is not achieved with muscle relaxants and benzodiazepines
C. IVIG dose does not exceed initial dose of 2,000 mg/kg

MAINTENANCE

A. With an objective benefit the IVIG could continue at REDUCED dose, and progressive tapering.
   **Maintenance Dose IV: Titrated to the lowest possible dose (less than initial dose) every 3 to 6 weeks (administered in divided doses)*
B. Maintenance therapy should be at the lowest dose of IVIG possible.

FDA Approved Dose and Indication

Product Name Formulation Route of Administration	FDA Approved Indications	FDA Approved Doses	Product Specifics
• **Asceniv** • 10% (5 gm bottle) • IV infusion	Primary Immunodeficiencies	300 – 800 mg/kg every 3 – 4 weeks	**IgA:** ≤200 mcg/mL **Osmolality:** 510 mOsm/kg **Stabilizer:** Glycine and polysorbate 80
• **Bivigam** • 10% liquid (5 gm • bottle) IV infusion	Primary Immunodeficiencies	300 - 800 mg/kg every 3-4 weeks	**IgA:** ≤200 mcg/mL **Osmolality:** 510 mOsm/kg **Stabilizer:** glycine
• **Carimune NF** • Powder for dilution to 3%, 6%, 9%, or 12% (6, 12 gm bottles) • IV infusion	Primary Immunodeficiencies	400 - 800 mg/kg every 3 – 4 weeks	**IgA:** 1000 to 2000 mcg/mL (6% solution) **Osmolality:** 192 to 1074 mOsm/kg *(depends on diluent and final concentration)*[10] **Stabilizer:** sucrose
	Idiopathic thrombocytopenic purpura	**Induction:** 400 mg/kg on 2 – 5 consecutive days **Maintenance:** 400 mg – 1000 mg PRN platelet count ≥ 30,000/mm^3 and/or to control significant bleeding.	
• **Cutaquig** • 16.5% (1 g, 1.65 g, 2 g, 3.3 g, 4 g, 8 g bottles) • Subcutaneous infusion only	Primary Immunodeficiencies	**Patients switching from IGIV therapy:** Initial Weekly dose = Previous IGIV dose (gm) # of weeks between doses X (1.40)	**IgA:** ≤ 600 mcg/mL **Osmolality:** 310 - 380 mOsmol/kg **Stabilize:** Maltose
		Patients switching from another IG SubQ product: Weekly dose is the same as the prior subQ weekly dose	
• **Cuvitru**	Primary Immunodeficiencies	**Patients switching from IGIV therapy:** Initial Weekly dose =	**IgA:** 80 mcg/mL

• 20% liquid (1, 2, 4, 8, 10 gm bottles) • Subcutaneous infusion only		Previous IGIV or HYQVIA dose (gm): # of weeks between doses X (1.30) **Patients switching from another IG SubQ product:** Weekly dose is the same as the prior subQ weekly dose	**Osmolality:** 280 to 292 mOsm/kg **Stabilizer:** glycine
• **Flebogamma 5% DIF** • 5% liquid (0.5, 2.5, 5, 10, 20 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks	**IgA:** <50 mcg/mL **Osmolarity:** 240 to 370 mOsm/kg **Stabilizer:** sorbitol
• **Flebogamma 10% DIF** • 10% liquid (5, 10, 20 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks	**IgA:** <32 mcg/mL **Osmolarity:** 240 to 370 mOsm/L **Stabilizer:** sorbitol
	Idiopathic thrombocytopenia	1000 mg/kg daily x 2 days	
• **Gammagard Liquid** • 10% liquid (1, 2.5, 5, 10, 20, 30 gm bottles) • IV or subcutaneous *(for primary Immunodeficiencies only)* infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks based upon response	**IgA:** 37 mcg/mL **Osmolality:** 240 to 300 mOsm/kg **Stabilizer:** glycine
	Multifocal motor neuropathy	500 – 2400 mg/kg/month based upon response	
• **Gammagard S/D4** • Powder for dilution to 5% or 10% (5, 10 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks	**IgA:** 1 mcg/mL (5% solution) **Osmolality:** 636 mOsm/L11 (5% solution) **Stabilizer:** glycine
	Idiopathic thrombocytopenic purpura	1,000 mg/kg (Maximal 3 doses on alternate days)	
	Chronic lymphocytic leukemia	400 mg/kg every 3 – 4 weeks	
	Kawasaki syndrome	1,000 mg/kg or 400 mg/kg for 4 consecutive days	
• **Gammaked** • 10% liquid • IV or subcutaneous *(for primary*	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks **(IV)** 1.37 X current iv dose **(SQ)**	**IgA:** 46 mcg/mL **Osmolality:** 258 mOsm/kg **Stabilizer:** glycine

Immunodeficiencies only) infusion • (1, 5, 10, 20 gm)	Idiopathic thrombocytopenic purpura	1,000 mg/kg/day X 2 days **OR** 400 mg/kg/day X 5 days	
	Chronic inflammatory demyelinating polyneuropathy	**Loading:** 2,000 mg/kg (divided over 2 – 4 consecutive days) **Maintenance:** 1,000 mg/kg (given over 1 day or divided over 2 consecutive days) every 3 weeks	
• **Gammaplex** • 5% liquid (5, 10, 20 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 800 mg/kg every 3 – 4 weeks	**IgA:** <10 mcg/mL **Osmolality:** 420 to 500 mOsm/kg **Stabilizer:** glycine and others
	Idiopathic thrombocytopenic purpura	1,000 mg/kg every for 2 consecutive days	
• **Gamunex-C** • 10% liquid (1, 2.5, 5, 10, 20, 40 gm bottles) • IV or subcutaneous *(primary Immunodeficiencies only)* infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks **(IV)** 1.37 X current iv dose **(SQ)**	**IgA:** 46 mcg/mL **Osmolality:** 258 mOsm/kg **Stabilizer:** glycine
	Idiopathic thrombocytopenic purpura	1,000 mg/kg/day X 2 days **OR** 400 mg/kg/day X 5 days	
	Chronic inflammatory demyelinating polyneuropathy	**Loading:** 2,000 mg/kg (divided over 2 – 4 consecutive days) **Maintenance:** 1,000 mg/kg (given over 1 day or divided over 2 consecutive days) every 3 weeks	
• **Hizentra** • 20% (1,2,4,10 gm) • Subcutaneous infusion only	Primary Immunodeficiencies	**Patients switching from IGIV therapy:** Initial Weekly dose = Previous IGIV dose (gm) # of weeks between doses X (1.37) **Patients switching from another IG**	**IgA:** ≤50 mcg/mL **Osmolality:** 380 mOsm/kg **Stabilizer:** Proline

		SubQ product: Weekly dose is the same as the prior subQ weekly dose	
	Chronic inflammatory demyelinating polyneuropathy (maintenance)	May qualify under member's pharmacy benefit	
• **HyQvia** • 10% liquid (2.5, 5, 10, 20, 30 gm bottles) • Subcutaneous infusion only	Primary Immunodeficiencies	**Initial ramp-up schedule:** See manufacturer's labeling **Patients naive to IgG therapy or switching from IG SubQ therapy**: 300 – 600 mg/kg every 3 – 4 weeks **(SQ),** after the initial dose ramp-up **Patients switching from IGIV therapy:** use same dose and frequency as previous IV treatment after the initial dose ramp-up	**IgA:** 37 mcg/mL **Osmolality:** 240 to 300 mOsm/kg **Stabilizer:** glycine
• **Octagam 5%** • 5% liquid (1, 2.5, 5, 10, 25 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks	**IgA:** ≤200 mcg/mL **Osmolality:** 310 to 380 mOsm/kg **Stabilizer:** maltose
• **Octagam 10%** • 10% liquid (2, 5, 10, 20, 30 gm bottles) • IV infusion	Idiopathic thrombocytopenic purpura	1,000 mg/kg/day X 2 days	**IgA:** 106 mcg/mL **Osmolality:** 310 to 390 mOsm/kg **Stabilizer:** maltose
• **Panzyga** • 10% liquid (1, 2.5, 5, 10, 20, and 30 gm bottles) • IV infusion	Primary Immunodeficiencies	300 – 600 mg/kg every 3 – 4 weeks	**IgA:** 100 mcg/mL **Osmolality:** 240 to 310 mOsm/kg **Stabilizer:** Glycine
	Idiopathic thrombocytopenic purpura	1,000 mg/kg/day X 2 days	
• **Privigen**	Primary Immunodeficiencies	200 – 800 mg/kg every	

• 10% liquid (5, 10, 20, 40 gm bottles) • IV infusion		3 – 4 weeks	**IgA:** ≤25 mcg/mL **Osmolality:** 320 mOsm/kg **Stabilizer:** L-proline
	Idiopathic thrombocytopenic purpura	1,000 mg/kg/day X 2 days	
	Chronic inflammatory demyelinating polyneuropathy	**Loading:** 2,000 mg/kg (divided over 2 – 5 consecutive days) **Maintenance:** 1,000 mg/kg (given over 1 day or divided over 2 consecutive days) every 3 weeks	
• **Xembify** • 20% (1,2,4,10 gm bottles) • Subcutaneous infusion only	Primary Immunodeficiencies	**Patients switching from IGIV therapy:** Initial Weekly dose = Previous IGIV dose (gm) # of weeks between doses X (1.37) **Patients switching from another IG SubQ product:** Weekly dose is the same as the prior subQ weekly dose	**IgA:** Not listed **Osmolality:** 280 - 404 mOsm/kg **Stabilizer:** Glycine

General Background

Intravenous Immune Globulin (IVIG) is a solution of human immunoglobulin that contains a broad range of antibodies which specifically act against bacterial and viral antigens. It acts to provide adequate concentrations of antibodies against a broad range of pathogens. Thus, the use of intravenous immune globulin should be reserved for patients with serious defects of antibody function.

IVIG carries the potential risk of transmitting infections because it is derived from pooled human donor blood. Infusion-related reactions including headache, fever, chills, muscle pain, chest discomfort, fatigue and/or nausea occur in 25 – 35 % of patients receiving IVIG treatment. There is a possibility of developing severe blood clots in some cases.

There are several IVIG products with varying concentrations of immunoglobulin G (IgG) and immunoglobulin A (IgA); however, the exact mechanism of action is unknown. It is likely that there are multiple mechanisms of IVIG action that may be specific to each autoimmune disease.[10]

Both National Coverage Determinations (NCD) and Local Coverage Determinations (LCD) applicable to Texas are available at the time of latest policy revision.

PLEASE NOTE: Hizentra® is listed on the LCA: Self-Administered Drug Exclusion List (A53127) and is not a covered benefit for Medicare Part B for non-Primary Immunodeficiency diagnosis. Requests for this product for non-primary immune deficiency diagnosis will be redirected to the member's pharmacy benefit[9].

HCPCS Code

HCPCS Code	Description
J1554	Injection, Asceniv, 500 mg
J1556	Injection, Bivigam, 500 mg
J1566	Injection, Carimune NF, 500 mg
J1555	Injection, Cuvitru, 100 mg
J1572	Injection, Flebogamma, 500 mg
J1569	Injection, Gammagard Liquid, 500 mg
J1561	Injection, Gamunex-C/Gammaked, 500 mg
J1557	Injection, Gammaplex, 500 mg
J1559	Injection, Hizentra, 100 mg
J1575	Injection, HyQvia, 100 mg
J1568	Injection, Octagam, 500 mg
J1599	Injection, Panzyga, 500 mg
J1459	Injection, Privigen, 500 mg
J1558	Injection, Xembify, 100 mg
J1551	Injection, Cutaquig 100 mg

Acronyms

IVIG = Intravenous Immune Globulin

NCD = National Coverage Determination

LCD = Local Coverage Determinations

CMS = Centers for Medicare and Medicaid

IgA = Immunoglobulin A

IgG = Immunoglobulin G

ITP = Idiopathic Thrombocytopenic Purpura

References

1. Immune Globulin In: DRUGDEXR System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/micromedex2/librarian/CS/6D7200/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/5258F1/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=Immune+Globulin&fromInterSaltBase=true&UserMdxSearchTerm=%24userMdxSearchTerm&false=null&=null#. Assessed July 30, 2021
2. CMS IOM Publication 100-02, *Medicare Benefit Policy Manual.* Chapter 15, Covered Medical and Other Health Services, Section 50: Drugs and Biologicals and Section 60: Services and Supplies Furnished Incident to a Physician's/NPP's Professional Service
3. CMS IOM Publication 100-03, *Medicare National Coverage Determinations (NCD) Manual,* Chapter 1, Part 4, Section 250.3: Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases. Viewed online at https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=158&ncdver=1&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD&PolicyType=Both&s=All&KeyWord=Intravenous+Immune+Globulin&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=MAAAABAAAAAA&. Accessed June 21, 2021
4. Medicare Benefit Policy Manual; Chapter 15; Covered Medical and Other Health Services; 50.6 Coverage of IVIG for Treatment of Primary Immune Deficiency Diseases in the Home. Viewed online at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf Accessed on June 21, 2021
5. CMS Local Coverage Determination (LCD): Intravenous Immune Globulin (IVIG) (L35093). Effective 11/14/2019. Accessed at https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35093&ver=100&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD&PolicyType=Both&s=All&KeyWord=Intravenous+Immune+Globulin&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=MAAAABAAAAAA&. Accessed on June 21, 2021
6. Comparison of IVIG products. Pharmacist Letter, December 2016. Available at https://pharmacist.therapeuticresearch.com/Content/Segments/PRL/2011/Nov/Comparison-of-IVIG-Products-3766. Assessed on July 30, 2021
7. CMS Benefit Policy Manual Chapter 15; 50 Drugs and Biologicals, Section 4.5 Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen. Accessed at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf. Accessed on June 21, 2021
8. CMS Local Coverage Article (LCA): Self-Administered Drug Exclusion List (A52800). Effective 04/01/2021. Accessed at https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52800. Accessed on July 30, 2021.

9. CIDP and PI Access and Billing Codes: Diagnostic and billing codes for Hizentra therapy. Access at *https://www.hizentra.com/hcp/access-billing-codes*. Accessed June 21, 2021
10. "IVIG (Intravenous Immunoglobulin)." Rheumatologic Dermatology Society, North America. Accessed at https://www.rheumaderm-society.org/ivig/. Accessed on June 21, 2021
11. EFNS/PNS Guidelines (J Peripheral Nervous System 2010; 15: 1-9), Koski Guidelines (J Neuro Sci. 2009; (1-2): 1-8), or AAN Guidelines (Neurology. 2012; 78: 1009-1015).