Neighborhood Health Plan OF RHODE ISLAND™
910 Douglas Pike, Smithfield, RI 02917 : 1-800-963-1001 : nhpri.org

SCIG (immune globulin SC): Hizentra®, Gammagard Liquid ERC®, Gamunex®-C, Gammaked®, Hyqvia®, Cuvitru®, Cutaquig®, Xembify® (Subcutaneous)

Effective Date: 01/01/2020
Review Date: 10/02/2019, 1/3/2019, 1/15/2020, 6/22/2020, 6/24/2021, 5/5/2022, 3/2/2023, 6/29/2023, 12/21/2023, 01/10/2024, 09/04/2024, 07/02/2025, 07/21/2026

Scope: Medicaid*, Commercial, Medicare

***(Medication only available on the Medical Benefit.)**

I. Length of Authorization

Initial coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Drug Name	Dose/ week	Dose/28 days
Hizentra	46 g	184 g
Gamunex-C & Gammaked	42 g	168 g
Gammagard liquid ERC	42 g	168 g
HyQvia	40 g	160 g
Cuvitru & Cutaquig	40 g	160 g
Xembify	42 g	168 g

B. Max Units (per dose and over time) [HCPCS Unit]:

Drug Name	Billable units/28 days
Hizentra	1680 (All other indications)
	1840 (CIDP)
Gamunex-C, Gammaked,	336
Gammagard liquid ERC	336
HyQvia	1200
Cuvitru & Cutaquig	1600
Xembify	1680

III. Initial Approval Criteria

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

- Baseline values for BUN and serum creatinine are obtained within 30 days of request; **AND**
- If requesting non preferred subcutaneous immune globulin formulations, such as Cuvitru, Cutaquig, Xembify, Hizentra or Hyqvia, the member must have failure or intolerance to the following preferred formulations: Gammaked/Gamunex-C or Gammagard liquid ERC (for members that are currently on treatment with Cuvitru, Cutaquig, Xembify, Hizentra or Hyqvia, they can remain on treatment)

Coverage is provided in the following conditions:

Primary Immunodeficiency (PID) †

Such as: Wiskott -Aldrich syndrome, 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) [**list not all inclusive**]

- Member is at least 2 years of age; **AND**
- Member has an IgG level <200 mg/dL **OR**
- Member meets **both** of the following
  - Member has a history of multiple hard to treat infections as indicated by at least **one** of the following:
    - Four or more ear infections within 1 year
    - Two or more serious sinus infections within 1 year
    - Two or more months of antibiotics with little effect
    - Two or more pneumonias within 1 year
    - Recurrent, deep skin or organ abscesses
    - Persistent thrush in mouth or fungal infection on the skin
    - Need for intravenous antibiotics to clear infections
    - Two or more deep-seated infections including septicemia
    - Family history of PID; **AND**
  - The member has a deficiency in producing antibodies in response to vaccination; **AND**
    - Titers were drawn before challenging with vaccination; **AND**
    - Titers were drawn between 4 and 8 weeks of vaccination

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and Hyqvia ONLY] †

- Member is at least 18 years of age; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.); **AND**
  - Used as initial maintenance therapy for prevention of disease relapses after treatment and stabilization with intravenous immunoglobulin (IVIG)§; **OR**
  - Used for re-initiation of maintenance therapy after experiencing a relapse and requiring re-induction therapy with IVIG (see Section IV for criteria)

§ Initial IVIG criteria used for determination of coverage: *(Reference Use Only)*

- Member's disease course is progressive or relapsing and remitting for 2 months or longer; **AND**
- Member has abnormal or absent deep tendon reflexes in upper or lower limbs; **AND**
- Electrodiagnostic testing indicating demyelination:
  - Partial motor conduction block in at least two motor nerves or in 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
  - Distal CMAP duration increase in at least 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
  - Abnormal temporal dispersion conduction must be present in at least 2 motor nerves; **OR**
  - Reduced conduction velocity in at least 2 motor nerves; **OR**
  - Prolonged distal motor latency in at least 2 motor nerves; **OR**
  - Absent F wave in at least two motor nerves plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
  - Prolonged F wave latency in at least 2 motor nerves; **AND**
- Member is refractory or intolerant to corticosteroids (e.g., prednisolone, prednisone, etc.) given in therapeutic doses over at least three months; **AND**
- Baseline in strength/weakness has been documented using an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

† FDA Approved Indication(s)

IV. Renewal Criteria

Coverage can be renewed for 1 year based upon the following criteria:

- Member continues to meet criteria identified in section III; **AND**
- 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**

- BUN and serum creatinine obtained within the last 6 months and the concentration and rate of infusion have been adjusted accordingly; **AND**

Primary Immunodeficiency (PID)

- Disease response as evidenced by one or more of the following:
    - Decrease in the frequency of infection
    - Decrease in the severity of infection

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and HyqviaONLY]

- Renewals will be authorized for members that have demonstrated a beneficial clinical response to maintenance therapy, without relapses, based on an objective clinical measuring tool [e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.]; **OR**
- Member is re-initiating maintenance therapy after experiencing a relapse while on Hizentra or Hyqvia**; AND**
    - Member improved and stabilized on IVIG treatment: **AND**
    - Member was NOT receiving maximum dosing of Hizentra or Hyqvia prior to relapse

V. Dosage/Administration

Dosing should be calculated using adjusted body weight if one or more of the following criteria are met:

- Patient's body mass index (BMI) is 30 kg/m^2 or more; **OR**
- Patient's actual body weight is 20% higher than his or her ideal body weight (IBW)

Use the following dosing formulas to calculate the adjusted body weight (round dose to nearest 5 gram increment in adult patients)
Dosing formulas
BMI = 703 x (weight in pounds/height in inches^2)
IBW(kg) for males = 50 + [2.3 (height in inches – 60)]
IBW(kg) for females = 45.5 + [2.3 x (height in inches – 60)]
Adjusted body weight = IBW + 0.5 (actual body weight – IBW)

This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

Indication	Dose
Chronic Inflammatory Demyelinating Polyneuropathy (CIPD)	<u>Hizentra:</u> ▪ Initiate therapy 1 week after the last IVIG dose ▪ The recommended subcutaneous dose is 0.2 g/kg (1 mL/kg) body weight per week, administered in 1 or 2 sessions over 1 or 2 consecutive days. ▪ If CIDP symptoms worsen, consider increasing the dose to 0.4 g/kg (2 mL/kg) body weight per week, administered in 2 sessions over 1 or 2 consecutive days.

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td></td><td>

If CIDP symptoms worsen on the 0.4 g/kg body weight per week dose, consider re-initiating therapy with an IVIG while discontinuing Hizentra.

<u>HyQqvia:</u>

Patients must be on stable doses of IVIG prior to starting HyQvia.
Before initiating therapy with Hyqvia, calculate the weekly equivalent dose to plan for the ramp-up schedule (see table below): previous IVIG dose (g)/number of weeks between IVIG doses
The sStarting dose and dosing frequency of Hyqvia is the same as the patient's previous IVGIGV treatment.
The typical dosing interval range in the clinical trial for Hyvia was 4 weeks. For patients with less frequent IVGIGV dosing (greater than 4 weeks), the dosing interval can be converted to 3 or 4 weeks while maintaining the same monthly equivalent IgG dose.
Administer the calculated one-week dose (1st infusion) 2 weeks after the last IVGIGV infusion. One week after the first Hyqvia dose, administer another weekly equivalent dose (2nd infusion).
A ramp-up period can take up to 9 weeks, depending on the dosing interval and tolerability (see table below)

<table>
<tr><th colspan="3">HyQvia Dose Ramp-up Schedule</th></tr>
<tr><th>Week*</th><th>Infusion Number</th><th>Dose Interval</th></tr>
<tr><td>1</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>2</td><td>1st infusion</td><td>1-week-doseDose in Grams X 0.67</td></tr>
<tr><td>3</td><td>2nd infusion</td><td>1-week-doseTotal Dose in Grams</td></tr>
<tr><td>4</td><td>3rd infusion</td><td>2-week-doseTotal Dose in Grams</td></tr>
<tr><td>5</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>6</td><td>4th infusion</td><td>3-week-dose</td></tr>
<tr><td>7</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>8</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>9</td><td>5th infusion</td><td>4-week-dose</td></tr>
</table>

– *Clock starts one week after the last IVIG IV dose is administered. Week 1 is the week that starts one week after the last IVIG IV dose.

</td></tr>
<tr><td>Primary immune deficiency (PID)</td><td>
<u>Hizentra:</u>

Switching from IVIG

Initiate therapy 1 to 2 weeks after the last IVIG dose
Weekly dose: 1.37*(previous IVIG dose (g)/number of weeks between IVIG doses)
May be administered from daily up to every two weeks (biweekly)
Biweekly dose: twice the weekly dose (using calculation above)
Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week

</td></tr>
</table>

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td></td><td>

Switching from SCIG

Initiate therapy 1 week after the last SCIG dose
Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams)
Biweekly dose: multiply the prior weekly dose by 2

Frequent dosing (2-7 times per week): divide the prior weekly dose by the desired number of times per week

<u>Gamunex-C/Gammaked/Gammagard Liquid ERC:</u>

Switching from IVIG

Initiate therapy 1 week after the last IVIG dose
Weekly dose: 1.37*(previous IVIG dose(g)/number of weeks between IVIG doses)

<u>HyQvia</u>:

Naïve to IgG or switching from SCIG: 300 to 600 mg/kg at 3 to 4 week intervals after initial ramp-up (see table below)
Switching from IVIG: use the same dose and frequency as the previous IV treatment after initial ramp-up (see table below)

<table>
<tr><th colspan="4">HyQvia Initial Treatment Interval/Dosage Ramp-up Schedule</th></tr>
<tr><th>Week</th><th>Infusion Number</th><th>3-week treatment interval</th><th>4-week treatment interval</th></tr>
<tr><td>1</td><td>1st infusion</td><td>Dose in Grams X 0.33</td><td>Dose in Grams X 0.25</td></tr>
<tr><td>2</td><td>2nd infusion</td><td>Dose in Grams X 0.67</td><td>Dose in Grams X 0.50</td></tr>
<tr><td>4</td><td>3rd infusion</td><td>Total Dose in Grams</td><td>Dose in Grams X 0.75</td></tr>
<tr><td>7</td><td>4th infusion</td><td>Total Dose in Grams</td><td>Total Dose in Grams</td></tr>
</table>
<u>Xembify:</u>

Switching from IVIG :

Start treatment one week after the last IVIG infusion.
Weekly dose: 1.37*(previous monthly (or every 3- week) IVIG dose in grams)/number of weeks between IVIG doses)

To convert the dose in grams to mL, multiply the calculated initial SQ dose (in grams) by 5
Provided the total weekly dose is maintained, any dosing interval from daily up to weekly will achieve similar systemic IgG exposure when administered regularly at steady-state.

Switching from SCIG

Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams)

<u>Cuvitru:</u>
Switching from IVIG or HyQvia:

Initiate therapy 1 week after the last IVIG dose

</td></tr>
</table>

Indication	Dose
	○ Weekly dose: 1.30*(previous IVIG or HyQvia dose (g)/number of weeks between IVIG or HyQvia doses) ○ May be administered from daily up to every two weeks (biweekly) ○ Biweekly dose: twice the weekly dose (using calculation above) ○ Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week ▪ Switching from SCIG ○ Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams) ○ May be administered from daily up to every two weeks (biweekly) ○ Biweekly dose: multiply the prior weekly dose by 2 ○ Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week
	Cutaquig: (*Start treatment one week after the last IVIG or SCIG infusion. Ensure that patients have received IVIG or SCIG treatment at regular intervals for at least 3 months*) ▪ Switching from IVIG ○ Weekly dose: 1.30*(previous IVIG dose (g)/number of weeks between IVIG doses) ○ May be administered from daily up to every two weeks (biweekly) ○ Biweekly dose: multiply the calculated weekly dose by 2 ○ Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week ▪ Switching from SCIG ○ Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams) ○ May be administered from daily up to every two weeks (biweekly) ○ Biweekly dose: multiply the prior weekly dose by 2 ▪ Frequent dosing (2-7 times per week): divide the prior weekly dose by the desired number of times per

Dosing for immunoglobulin products is highly variable depending on numerous patient specific factors, indication(s), and the specific product selected. For specific dosing regimens refer to current prescribing literature.

VI. Billing Code/Availability Information

HCPCS code & NDC:

Drug Name	Manufacturer	HCPCS Code or CPT Code	1 Billable unit	NDC	IgG (grams) per SDV	Volume (mL)
Hizentra 20%	CSL Behring AG	J1559 – Injection, immune globulin (Hizentra), 100 mg	100 mg	44206-0451-01	1	5
				44206-0452-02	2	10

Drug Name	Manufacturer	HCPCS Code or CPT Code	1 Billable unit	NDC	IgG (grams) per SDV	Volume (mL)
				44206-0454-04	4	20
				44206-0455-10	10	50
Gammaked 10%	Kedrion Biopharma, Inc.	J1561 Injection, immune globulin, (Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg	500 mg	76125-0900-01	1	10
				76125-0900-25	2.5	25
				76125-0900-50	5	50
				76125-0900-10	10	100
				76125-0900-20	20	200
Gamunex-C 10%	Grifols Therapeutics	J1561 – Injection, immune globulin, (Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg	500 mg	13533-0800-12	1	10
				13533-0800-15	2.5	25
				13533-0800-20	5	50
				13533-0800-71	10	100
				13533-0800-24	20	200
				13533-0800-40	40	400
Gammagard Liquid ERC	Baxter Healthcare Corporation	J1569 – Injection, immune globulin, (Gammagard liquid), non-lyophilized, (e.g. liquid), 500 mg	500 mg	00944-2700-02	1	10
				00944-2700-03	2.5	25
				00944-2700-04	5	50
				00944-2700-05	10	100
				00944-2700-06	20	200
				00944-2700-07	30	300
HyQvia 10% (with Recombinant Human Hyaluronidase 160 U/mL)	Baxter Healthcare Corporation	J1575 – Injection, immune globulin/hyaluronidase, (Hyqvia), 100 mg immune globulin	100 mg	00944-2510-02	2.5	25
				00944-2511-02	5	50
				00944-2512-02	10	100
				00944-2513-02	20	200
				00944-2514-02	30	300
Cuvitru 20%	Baxalta US Inc.	J1555 – Injection, immune globulin (Cuvitru), 100 mg	100 mg	00944-2850-01	1	5
				00944-2850-03	2	10
				00944-2850-05	4	20
				00944-2850-07	8	40
Cutaquig 16.5%	Octapharma	J1551	N/A	68892-0810-01	1	6
				68892-0810-02	1.65	10
				68892-0810-03	2	12
				68892-0810-04	3.3	20

Drug Name	Manufacturer	HCPCS Code or CPT Code	1 Billable unit	NDC	IgG (grams) per SDV	Volume (mL)
				68892-0810-05	4	24
				68892-0810-06	8	48
Xembify 20%	Grifols	90284; J1558	N/A	13533-0810-05	1	5
				13533-0810-10	2	10
				13533-0810-20	4	20
				13533-0810-50	10	50
Immune Globulin, Human, Subcutaneous	N/A	J3590 – unclassified biologic; C9399 – unclassified drug or biological	N/A	N/A	N/A	N/A
		90284 – immune globulin (SCIg), human, for use in subcutaneous infusions				

VII. Summary of Evidence

Hizentra:

Hizentra is a 20% subcutaneous immune globulin (SCIG) indicated for maintenance therapy in primary humoral immunodeficiency (PI) and chronic inflammatory demyelinating polyneuropathy (CIDP). In PI, efficacy was established in a prospective, open-label, multicenter trial demonstrating protection from serious bacterial infections (SBI) with a mean rate of 0.04 SBIs/patient-year. In CIDP, the PATH study demonstrated that maintenance therapy with Hizentra reduced relapse rates versus placebo. Subcutaneous dosing allowed for flexible self-administration. Common adverse reactions (≥5%) included injection-site reactions, headache, diarrhea, fatigue, back pain, and cough. Hizentra contains no sucrose and is stabilized with L-proline.

Gammagard Liquid ERC:

Gammagard Liquid ERC is SCIG formulation indicated for primary humoral immunodeficiency (PI) in adults and children ≥2 years. A pivotal study demonstrated bioequivalence of subcutaneous and intravenous dosing, with maintained serum IgG trough levels and a serious bacterial infection rate of 0.02 per patient-year. Subcutaneous dosing was individualized based on a 1.37 conversion factor from the IV dose and was well-tolerated. The most common adverse reactions (≥5%) with subcutaneous use were infusion site reactions, headache, fatigue, arthralgia, and fever. Gammagard Liquid ERC is free of sucrose, preservatives, and proline.

Gamunex-C (SC):
Gamunex-C is a 10% immune globulin for intravenous and subcutaneous administration, approved for treatment of PI in patients aged 2 years and older. SCIG dosing is based on a 1.37 conversion factor from the IV dose, with weekly administration. Clinical trials demonstrated effective IgG maintenance and protection against serious bacterial infections. Efficacy data showed a mean SBI rate well below 1 per patient-year. Common adverse events (≥5%) with subcutaneous use included infusion site reactions, headache, fatigue, and fever. Gamunex-C is stabilized with glycine and does not contain sucrose.

Gammaked (SC):
Gammaked is a 10% caprylate/chromatography purified immune globulin administered subcutaneously for the treatment of primary humoral immunodeficiency (PI) in patients ≥2 years old. SCIG administration follows a 1.37 conversion factor from IVIG dosing to ensure systemic IgG exposure is equivalent. Clinical trials demonstrated consistent serum IgG levels and a low rate of serious bacterial infections. Common adverse effects (≥5%) with subcutaneous use included infusion site reactions, headache, fatigue, arthralgia, and fever. Gammaked is sucrose-free and stabilized with glycine.

Hyqvia:
Hyqvia is a dual-component product containing a 10% immune globulin (IG) solution and recombinant human hyaluronidase for subcutaneous administration, indicated for primary humoral immunodeficiency (PI) in adults and children aged 2 years and older. In a pivotal study of 83 patients, Hyqvia demonstrated a serious bacterial infection (SBI) rate of 0.025 per patient-year, meeting FDA efficacy benchmarks. The recombinant hyaluronidase facilitates dispersion and absorption, allowing monthly or biweekly SC administration of large volumes. Common adverse reactions (≥5%) included local infusion-site reactions, headache, fatigue, nausea, and fever. Hyqvia is free of sucrose and preservatives and enables less frequent dosing than conventional SCIG therapy.

Cuvitru:
Cuvitru is a 20% subcutaneous immune globulin (SCIG) used for the treatment of primary humoral immunodeficiency (PI) in patients aged 2 years and older. Clinical efficacy was demonstrated in two pivotal open-label trials (one in the U.S. and one in Europe) showing a combined serious bacterial infection (SBI) rate of 0.012 per patient-year. Cuvitru allows flexible dosing schedules ranging from daily to biweekly and supports high-volume, rapid infusion rates (up to 60 mL/hr/site). It is stabilized with L-proline and contains no sucrose, latex, or preservatives. Common adverse reactions (≥5%) were infusion-site reactions, headache, fatigue, diarrhea, and nausea.

Xembify:
Xembify is a 20% subcutaneous immune globulin (SCIG) indicated for the treatment of primary humoral immunodeficiency (PI) in patients aged 2 years and older. In a clinical trial of 49 subjects, the mean serious bacterial infection (SBI) rate was 0.011 per patient-year, demonstrating effective protection. Xembify supports flexible dosing schedules ranging from twice weekly to every two weeks, with infusion rates up to 25 mL/hr/site. It is stabilized with glycine and contains no sucrose or preservatives. Common adverse events (≥5%) include infusion site reactions, headache, diarrhea, fatigue, and nausea. Xembify allows for home-based self-administration and high infusion tolerance.

Cutaquig:
Cutaquig is a 16.5% subcutaneous immune globulin (SCIG) used for the treatment of primary humoral immunodeficiency (PI) in adults and pediatric patients ≥2 years. Clinical trials reported an SBI rate of 0.015 per patient-year, meeting the FDA standard of <1 SBI/year. Cutaquig allows flexible infusion volumes and frequencies, typically administered weekly. The product is stabilized with glycine and is free from sucrose and preservatives. Adverse reactions (≥5%) include local site reactions, headache, fatigue, pruritus, and fever. Cutaquig is administered at home via multiple infusion sites, offering convenience and steady IgG levels.

VIII. References

1. Xembify [package insert]. Triangle Park, NC; Grifols; March 2025. Accessed July 2026.
2. Cutaquig [package insert]. Stokholm, Sweden; Octapharma; November 2021. Accessed July 2026.
3. Hizentra [package insert]. Bern, Switzerland; CSL Behring AG; April 2023. Accessed July 2026.
4. HyQvia [package insert]. Westlake Village, CA; Baxter Healthcare Corporation; June 2026. Accessed July 2026.
5. Cuvitru [package insert]. Westlake Village, CA; Baxalta US Inc.; November 2025. Accessed July 2026.
6. Gammagard Liquid ERC [package insert]. Westlake Village, CA; Baxter Healthcare Corporation; December 2025. Accessed July 2026.
7. Gamunex®-C [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc.; April 2022. Accessed July 2026.
8. Gammaked™ [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc.; January 2020. Accessed July 2026.
9. Jeffrey Modell Foundation Medical Advisory Board, 2013. 10 Warning Signs of Primary Immunodeficiency. Jeffrey Modell Foundation, New York, NY
10. Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.
11. Orange JS, Ballow M, Stiehm, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: A working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol Vol 130 (3).
12. Bonilla FA, Khan DA, Ballas ZK, et al. Practice Parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol 2015 Nov;136(5):1186-205.e1-78.
13. Emerson GG, Herndon CN, Sreih AG. Thrombotic complications after intravenous immunoglobulin therapy in two patients. Pharmacotherapy. 2002;22:1638-1641.
14. Department of Health (London). Clinical Guidelines for Immunoglobulin Use: Update to Second Edition. August, 2011.
15. Provan, Drew, et al. "Clinical guidelines for immunoglobulin use." Department of Health Publication, London (2008).
16. Dantal J. Intravenous Immunoglobulins: In-Depth Review of Excipients and Acute Kidney Injury Risk. Am J Nephrol 2013;38:275-284.

17. Immune Deficiency Foundation. Diagnostic & Clinical Care Guidelines for Primary Immunodeficiency Diseases. 3rd Ed. 2015. Avail at: https://primaryimmune.org/sites/default/files/publications/2015-Diagnostic-and-Clinical-Care-Guidelines-for-PI_1.pdf.
18. Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence. J Allergy Clin Immunol. 2017 Mar;139(3S):S1-S46.
19. First Coast Service Options, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (L34007). Centers for Medicare & Medicaid Services, Inc. Updated on 08/12/2019 with effective date 08/13/2019. Accessed August 2019.
20. Alonso W, Vandeberg P, Lang J, et al. Immune globulin subcutaneous, human 20% solution (Xembify®), a new high concentration immunoglobulin product for subcutaneous administration. Biologicals. 2020;64:34-40.
21. Kobayashi RH, Gupta S, Melamed I, et al. Clinical Efficacy, Safety and Tolerability of a New Subcutaneous Immunoglobulin 16.5% (octanorm [cutaquig®]) in the Treatment of Patients with Primary Immunodeficiencies. Front Immunol. February 2019 | Volume 10 | Article 40.
22. van Schaik IN, Bril V, van Geloven N, et al. Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (CIDP), a multicenter randomised double-blind placebo-controlled trial: the PATH Study. Lancet Neurol. 2017;17(1):35-46.
23. Hagan JB, Fasano MB, Spector S, et al. Efficacy and safety of a new 20% immunoglobulin preparation for subcutaneous administration, IgPro20, in patients with primary immunodeficiency. J Clin Immunol. 2010;30(5):734-745.
24. Jolles S, Borte M, Nelson R, et al. Long-term efficacy, safety, and tolerability of Hizentra for treatment of primary immunodeficiency disease. Clin Immunol. 2014;150(2):161-169.
25. Wasserman RL, Melamed I, Nelson RP Jr, et al. Pharmacokinetics of subcutaneous IgPro20 in patients with primary immunodeficiency. Clin Pharmacokinet. 2011;50(6):405-414.
26. Wasserman RL, Melamed I, Kobrynski L, et al. Efficacy, Safety, and Pharmacokinetics of a 10% Liquid Immune Globulin Preparation (GAMMAGARD LIQUID, 10%) Administered Subcutaneously in Subjects with Primary Immunodeficiency Disease. J Clin Immunol. 2011 Mar 22. [Epub ahead of print]
27. Food and Drug Administration. Safety, efficacy, and pharmacokinetic studies to support marketing of immune globulin intravenous (human) as replacement therapy for primary humoral immunodeficiency. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/safety-efficacy-and-pharmacokinetic-studies-support-marketing-immune-globulin-intravenous-human. Accessed October, 2023
28. Wasserman RL, Melamed I, Stein MR, et al; and IGSC, 10% with rHuPH20 Study Group. Recombinant human hyaluronidase-facilitated subcutaneous infusion of human immunoglobulins for primary immunodeficiency. J Allergy Clin Immunol. 2012;130(4):951-957.
29. Suez D, Stein M, Gupta S, et al. Efficacy, safety, and pharmacokinetics of a novel human immune globulin subcutaneous, 20% in patients with primary immunodeficiency diseases in North America. J Clin Immunol. 2016;36(7):700-712.
30. Roifman CM, Schroeder H, Berger M, et al. Comparison of the efficacy of IGIV-C, 10% (caprylate/chromatography) and IGIV-SD, 10% as replacement therapy in primary immune deficiency: a randomized double-blind trial. Int Immunopharmacol. 2003;3(9):1325-1333.

31. Roifman CM, Schroeder H, Berger M, et al, and the IGIV-C in PID Study Group. Comparison of the efficacy of IGIV-C, 10% (caprylate/chromatography) and IGIV-SD, 10% as replacement therapy in primary immune deficiency: a randomized double-blind trial. Int Immunopharmacol. 2003;3:1325-1333.
32. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 3.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2023.
33. Chapel H, Dicato M, Gamm H, et al. Immunoglobulin replacement in patients with chronic lymphocytic leukaemia: a comparison of two dose regimes. Br J Haematol 1994 Sep;88(1):209-12. doi: 10.1111/j.1365-2141.1994.tb05002.x.
34. Grindeland JW, Grindeland CJ, Moen C, Leedahl ND, Leedahl DD. Outcomes Associated With Standardized Ideal Body Weight Dosing of Intravenous Immune Globulin in Hospitalized Patients: A Multicenter Study. Ann Pharmacother. 2020 Mar;54(3):205-212. doi: 10.1177/1060028019880300. Epub 2019 Oct 3.
35. Epland, K., Suez, D. & Paris, K. A clinician's guide for administration of high-concentration and facilitated subcutaneous immunoglobulin replacement therapy in patients with primary immunodeficiency diseases. Allergy Asthma Clin Immunol 18, 87 (2022). https://doi.org/10.1186/s13223-022-00726-7
36. Jeffrey Modell Foundation Medical Advisory Board, 2021. 10 Warning Signs of Primary Immunodeficiency. Jeffrey Modell Foundation, New York, NY. https://res.cloudinary.com/info4pi/image/upload/v1662306262/JMF_10_Signs_Generic_082421_v2_dcadf429cc.pdf?updated_at=2022-09-04T15:44:23.120Z. Accessed October 2023.
37. Van den Bergh PYK, van Doorn PA, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second revision. Eur J Neurol. 2021 Nov;28(11):3556-3583. Erratum in: Eur J Neurol. 2022 Apr;29(4):1288. PMID: 34327760.
38. Bril V, Hadden RDM, Brannagan TH 3rd, et al. Hyaluronidase-facilitated subcutaneous immunoglobulin 10% as maintenance therapy for chronic inflammatory demyelinating polyradiculoneuropathy: The ADVANCE-CIDP 1 randomized controlled trial. J Peripher Nerv Syst. 2023 Sep;28(3):436-449. doi: 10.1111/jns.12573. Epub 2023 Jul 6. PMID: 37314318.
39. Hassan S, Duff K, Wisseh S, et al. Rationale and Design of a Phase 3b Study of the Long-Term Tolerability and Safety of HyQvia in Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP): ADVANCE-CIDP 3 (4331). Neurology 2020-04-14 94(15_supplement): 4331 https://doi.org/10.1212/WNL.94.15_supplement.4331.
40. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Immune Globulin (A57778). Centers for Medicare & Medicaid Services, Inc. Updated on 07/14/2023 with effective date 07/01/2023. Accessed January 2024.
41. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Immune Globulin (A56786). Centers for Medicare & Medicaid Services, Inc. Updated on 07/14/2023 with effective date 07/01/2023. Accessed January 2024.

42. Wisconsin Physicians Service Insurance Corporation. Local Coverage Article: Billing and Coding: Immune Globulins (A57554). Centers for Medicare & Medicaid Services, Inc. Updated on 11/22/2022 with effective date 12/01/2022. Accessed January 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
B20	Human immunodeficiency virus [HIV] disease
D80.0	Hereditary hypogammaglobulinemia
D80.1	Nonfamilial hypogammaglobulinemia
D80.2	Selective deficiency of immunoglobulin A [IgA]
D80.3	Selective deficiency of immunoglobulin G [IgG] subclasses
D80.4	Selective deficiency of immunoglobulin M [IgM]
D80.5	Immunodeficiency with increased immunoglobulin M [IgM]
D80.7	Transient hypogammaglobulinemia of infancy
D81.0	Severe combined immunodeficiency [SCID] with reticular dysgenesis
D81.1	Severe combined immunodeficiency [SCID] with low T- and B-cell numbers
D81.2	Severe combined immunodeficiency [SCID] with low or normal B-cell numbers
D81.6	Major histocompatibility complex class I deficiency
D81.7	Major histocompatibility complex class II deficiency
D81.89	Other combined immunodeficiencies
D81.9	Combined immunodeficiency, unspecified
D82.0	Wiskott-Aldrich syndrome
D83.0	Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function
D83.2	Common variable immunodeficiency with autoantibodies to B- or T-cells
D83.8	Other common variable immunodeficiencies
D83.9	Common variable immunodeficiency, unspecified
G61.81	Chronic inflammatory demyelinating polyneuritis
G61.89	Other inflammatory polyneuropathies
G62.89	Other specified polyneuropathies

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations.		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
H, L	A56786	Novitas Solutions, Inc.
N	A57778	First Coast Service Options, Inc.
5, 8	A57554	Wisconsin Physicians Service Insurance Corporation (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Hizentra, Gammagard Liquid ERC, Gamunex-C, Gammaked, Hyqvia, Cuvitru, Cutaquig, and Xembify were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Hizentra, Gammagard Liquid, Gamunex-C, Gammaked, Hyqvia, Cuvitru, Cutaquig, and Xembify according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual

consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.