MEDICAL MUTUAL®

Drug Policy

Policy:	**201317-MRx**	**Initial Effective Date: 07/01/2013** **Annual Review Date: 02/20/2025** **Last Revised Date: 02/20/2025**
Code(s):	**HCPCS J1555, J1558, J1559, J1561, J1569, J1575, J1551, J3590, C9399**	
SUBJECT:	**Immune Globulins Subcutaneous (SCIG)** • **Cutaquig® (immune globulin subcutaneous [human] 16.5% solution – Octapharma USA, Inc.)** • **Cuvitru™ (immune globulin subcutaneous 20% solution – Baxalta US Inc)** • **Gammagard Liquid (immune globulin infusion 10% solution – Baxalta US Inc.)** • **Gammaked™. (immune globulin injection 10% caprylate/chromatography purified – Kedrion Biopharma, Inc. [manufactured by Grifols Therapeutics Inc])** • **Gamunex®-C (immune globulin injection 10% caprylate/chromatography purified – Grifols [manufactured by Grifols Therapeutics, Inc])** • **Hizentra® (immune globulin subcutaneous 20% liquid - CSL Behring)** • **HyQvia (immune globulin infusion 10% with recombinant human hyaluronidase – Baxalta US Inc.)** • **Xembify (Immune Globulin Subcutaneous, Human - klhw, 20%- Grifols Therapeutics LLC)**	

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

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, Gammagard liquid & Gammaked	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	1840 (CIDP) 1680 (PID)
Gamunex-C, Gammaked, & Gammagard liquid	336
Cuvitru & Cutaquig	1600

Drug Name	Loading Dose Billable units	Maintenance Dose Billable units/21 days
HyQvia (CIDP)	Week 1: 0 Week 2: 400 Week 3: 400 Week 4: 800 Week 6: 1200 Week 9: 1600	1600
HyQvia (PID)	Week 1: 300 Week 2: 600	1200
Xembify	180 daily for 5 days	1680

III. Initial Approval Criteria [1-8,12,15,18]

Coverage is provided in the following conditions:

- Baseline values for BUN and serum creatinine obtained within 30 days of request; **AND**

Primary Immunodeficiency (PID) † [1-8,11,12,18,35]

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]***

- Patient is at least 2 years of age; **AND**
  - Patient has an IgG level <200 mg/dL; **OR**
  - Patient meets both of the following:
    - Patient 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 the 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 patient 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] † Φ [3,4,21,36]

- Patient 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)

Acquired Immune Deficiency Secondary to Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) ‡ [31,32,35]

- Patient has an IgG level <200 mg/dL; **OR**

- Patient has an IgG level <500 mg/dL**; AND**
  - Patient has recurrent sinopulmonary infections requiring IV antibiotics or hospitalization; **OR**
- Patient meets both of the following:
  - Patient 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 the mouth or fungal infection on the skin
    - Need for intravenous antibiotics to clear infections
    - Two or more deep-seated infections including septicemia; **AND**
  - The patient 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

- Note: other secondary immunodeficiencies resulting in hypogammaglobulinemia and/or B-cell aplasia will be evaluated on a case-by-case basis
- ***§*** *Refer to the Immune Globulins medical necessity criteria (Document Number: IC-0071) for the relevant intravenous criteria requirements*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1-8,15,18,36]

- Coverage may be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant 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 HyQvia ONLY]**

- 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 (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.); **OR**
- Patient is re-initiating maintenance therapy after experiencing a relapse while on Hizentra or HyQvia**; AND**
  - Patient improved and stabilized on IVIG treatment: **AND**
  - Patient was NOT receiving maximum dosing of Hizentra or HyQvia prior to relapse

Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) [31,32]

- Disease response as evidenced by one or more of the following:
  - Decrease in the frequency of infection
  - Decrease in the severity of infection; **AND**
- Continued treatment is necessary to decrease the risk of infection

V. Dosage/Administration[1-8,13-15,31-34]

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 + 0.4 (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.

<table>
<tr><th>Indication</th><th>Dose ❖</th></tr>
<tr><td>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)</td><td>
<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.
▪ 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>HyQvia:</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 starting dose and dosing frequency of HyQvia is the same as the patient’s previous IVIG treatment.
▪ The typical dosing interval range in the clinical trial for HyQvia was 4 weeks. For patients with less frequent IVIG 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 IVIG 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-dose</td></tr>
<tr><td>3</td><td>2nd infusion</td><td>1-week-dose</td></tr>
<tr><td>4</td><td>3rd infusion</td><td>2-week-dose</td></tr>
<tr><td>5</td><td>No infusion</td><td>Not applicable</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Indication</th><th>Dose ❖</th></tr>
<tr><td></td><td>
<table>
<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 dose is administered. Week 1 is the week that starts one week after the last IVIG dose.
</td></tr>
<tr><td rowspan="2">Primary Immune Deficiency (PID) AND Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)</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

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

</td></tr>
<tr><td>
<u>Gamunex-C/Gammaked/Gammagard Liquid:</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)

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

<table>
<tr><th>Indication</th><th>Dose ❖</th></tr>
<tr><td></td><td>HyQvia:
▪ Naïve to immune globulin treatment 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)
NOTE: For patients previously on another IgG treatment, initiate therapy 1 week after the last infusion of IVIG or SCIG
<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>
</td></tr>
<tr><td></td><td>Xembify:
▪ Switching from IVIG
o Start treatment one week after the last IVIG infusion.
o Weekly dose: 1.37*[previous monthly (or every 3- week) IVIG dose in grams/number of weeks between IVIG doses]
o May be administered from daily up to every two weeks (biweekly)
o Biweekly dose: multiply the prior weekly dose by 2
o Frequent dosing (2-7 times per week): divide the prior weekly dose by the desired number of times per week
▪ Switching from SCIG
o Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams)
o May be administered from daily up to every two weeks (biweekly)
o Biweekly dose: multiply the prior weekly dose by 2
o Frequent dosing (2-7 times per week): divide the prior weekly dose by the desired number of times per week
▪ Treatment naïve
o Loading dose: 150 mg/kg/day for 5 consecutive days</td></tr>
</table>

Indication	Dose ❖
	○ Maintenance dose: 150 mg/kg/week - weekly administrations starts at Day 8 ○ May be administered from daily up to every two weeks (biweekly)
	Cuvitru: ▪ Switching from IVIG or HyQvia ○ Initiate therapy 1 week after the last IVIG or Hyqvia 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 prior weekly dose by the desired number of times per week

Indication	Dose ❖
	Cutaquig: ***NOTE:*** *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 o Weekly dose: 1.30*(previous IVIG dose (g)/number of weeks between IVIG doses) o May be administered from daily up to every two weeks (biweekly) o Biweekly dose: multiply the calculated weekly dose by 2 o Frequent dosing (2-7 times per week): divide the calculated weekly dose by the desired number of times per week ▪ Switching from SCIG o Weekly dose (in grams) should be same as the weekly dose of prior SCIG treatment (in grams) o May be administered from daily up to every two weeks (biweekly) o Biweekly dose: multiply the prior weekly dose by 2 o Frequent dosing (2-7 times per week): divide the prior weekly dose by the desired number of times per week

❖ *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(s) & NDC(s):

Drug Name*	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
Hizentra 20% (Vials)	CSL Behring AG	J1559 – Injection, immune globulin (Hizentra), 100 mg	100 mg	44206-0451-01	1	5
				44206-0452-02	2	10
				44206-0454-04	4	20
				44206-0455-10	10	50
Hizentra 20% (Prefilled Syringes)	CSL Behring AG	J1559 – Injection, immune globulin (Hizentra), 100 mg	100 mg	44206-0456-21	1	5
				44206-0457-22	2	10
				44206-0458-24	4	20

Drug Name*	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
				44206-0455-25	10	50
Gammaked 10%	Grifols Therapeutics	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 10%	Baxalta US Inc.	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)	Baxalta US Inc.	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
				00944-2850-09	10	50
				00069-1061-01	1	6

Drug Name*	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
Cutaquig 16.5%	Octapharma	J1551 – Injection, immune globulin (cutaquig), 100 mg	100 mg	00069-1802-01	1.65	10
				00069-1476-01	2	12
				00069-1960-01	3.3	20
				00069-1509-01	4	24
				00069-1965-01	8	48
Xembify 20%	Grifols	J1558 – Injection, immune globulin (Xembify), 100 mg	100 mg	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 biologics C9399 – unclassified drugs or biologicals	N/A	N/A	N/A	N/A

**90284 – immune globulin (SCIg), human, for use in subcutaneous infusions*

VII. References

1. Xembify [package insert]. Research Triangle Park, NC; Grifols Therapeutics, LLC; July 2024. Accessed July 2024.
2. Cutaquig [package insert]. Vienna, Austria; Octapharma; November 2021. Accessed September 2023.
3. Hizentra [package insert]. Bern, Switzerland; CSL Behring AG; April 2023. Accessed September 2023.
4. HyQvia [package insert]. Lexington, MA; Baxalta US Inc.; January 2024. Accessed January 2024.
5. Cuvitru [package insert]. Lexington, MA; Baxalta US Inc.; March 2023. Accessed September 2023.
6. Gammagard Liquid [package insert]. Lexington, MA; Baxalta US Inc.; March 2023. Accessed September 2023.
7. Gamunex®-C [package insert]. Research Triangle Park, NC; Grifols Therapeutics, LLC; January 2020. Accessed September 2023.
8. Gammaked [package insert]. Research Triangle Park, NC; Grifols Therapeutics, LLC; January 2020. Accessed September 2023.
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. 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.
20. 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.
21. 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.
22. 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.
23. 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.
24. 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.
25. 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]

26. 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
27. 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.
28. 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.
29. 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.
30. 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.
31. 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.
32. 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.
33. 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.
34. 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
35. 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.
36. 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.

37. 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.
38. 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.
39. 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.
40. 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.
41. 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 (All Products)

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

ICD-10	ICD-10 Description
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

Additional covered diagnosis codes applicable to Hizentra and Hyqvia ONLY:

ICD-10	ICD-10 Description
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. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims

payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**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,	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	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.
