

SCIG (immune globulin SQ): Hizentra®, Gammagard Liquid®, Gamunex®-C, Gammaked™, HyQvia®, Cuvitru®, Cutaquig®, Xembify® (Subcutaneous)

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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	Maintenance Dose
	Billable units	Billable units/21 days



HyQvia (CIDP)	Week 1: 0	1600	
	Week 2: 400		
	Week 3: 400		
	Week 4: 800		
	Week 6: 1200		
	Week 9: 1600		
HyQvia (PID)	Week 1: 300	1200	
	Week 2: 600		
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
 - o Patient has an IgG level <200 mg/dL; OR
 - o Patient meets both of the following:
 - Patient has a history of multiple hard to treat infections as indicated by at least <u>one</u> 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
 - O Used for re-initiation of maintenance therapy after experiencing a relapse and requiring reinduction 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 <u>both</u> of the following:
 - Patient has a history of multiple hard to treat infections as indicated by at least <u>one</u> 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

<u>Note</u>: 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:
 - o 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
 - o 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/m² 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 5gram increment in adult patients)

Dosing formulas
BMI = 703 x (weight in pounds/height in inches²)
IBW (kg) for males = $50 + [2.3 \text{ (height in inches} - 60)]$
IBW (kg) for females = $45.5 + [2.3 \text{ x (height in inches} - 60)]$
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.

Indication	Dose �				
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	 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) 				
	tolerabli	ity (see tabl	HyQvia Dose Ramp-up	Schedule	
		Week*	Infusion Number	Dose Interval	
		1	No infusion	Not applicable	
		2	1st infusion	1-week-dose	
		3	2 nd infusion	1-week-dose	
		4	$3^{ m rd}$ infusion	2-week-dose	

SCIG: Hizentra, Gammagard Liquid, Gamunex-C, Gammaked, HyQvia, Cuvitru, Cutaquig, Xembify

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Indication	Dose �				
		5	No infusion	Not applicable	
		6	4 th infusion	3-week-dose	
		7	No infusion	Not applicable	
		8	No infusion	Not applicable	
		9	$5^{ m th}$ infusion	4-week-dose	
			eek after the last IVIG dose after the last IVIG dose.	is administered. Week 1 is	the week
Primary Immune Deficiency (PID) AND Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphocytic	• Switchin	Weekly dose doses) May be adm: Biweekly dose Frequent dose desired num ng from SCIO Initiate ther Weekly dose treatment (in Biweekly dose desired num	apy 1 to 2 weeks after the last SO (in grams) see: multiply the prior week!	(g)/number of weeks betweek very two weeks (biweekly) sing calculation above) ivide the calculated weekly CIG dose as the weekly dose of prior s	dose by th
(SLL)	 Switching 	ng from IVIO	1		
	0		apy 1 week after the last IV : 1.37*(previous IVIG dose(TIG dose g)/number of weeks between	ı IVIG



Indication Dose 🌣 HvQvia: 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 HyQvia Initial Treatment Interval/Dosage Ramp-up Schedule Week 3-week treatment interval 4-week treatment interval **Infusion Number** 1st infusion Dose in Grams X 0.33 Dose in Grams X 0.25 1 2 2nd infusion Dose in Grams X 0.67 Dose in Grams X 0.50 3rd infusion Total Dose in Grams Dose in Grams X 0.75 4 7 4th infusion Total Dose in Grams Total Dose in Grams Xembify: 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

- Weekly dose: 1.37*[previous monthly (or every 3- week) IVIG dose in grams/number of weeks between IVIG doses]
- May be administered from daily up to every two weeks (biweekly)
- o 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
- 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)
 - o 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
- Treatment naïve
 - o Loading dose: 150 mg/kg/day for 5 consecutive days
 - 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
 - o 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)
 - o Biweekly dose: twice the weekly dose (using calculation above)



Indication	Dose *
	o 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)
	o May be administered from daily up to every two weeks (biweekly)
	o 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
	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)
	 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
	 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)
	o 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

❖ 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)
				44206-0451-01	1	5
Hizentra 20%	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	J1559 — Injection, immune	1 100 mg	44206-0452-02	2	10
(Vials)		globulin (Hizentra), 100 mg		44206-0454-04	4	20
				44206-0455-10	10	50
			100 mg	44206-0456-21	1	5



Drug Name*	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
Hizentra 20%				44206-0457-22	2	10
(Prefilled	CSL Behring AG	J1559 – Injection, immune globulin (Hizentra), 100 mg		44206-0458-24	4	20
Syringes)	Au	growthin (minorital), 100 mg		44206-0455-25	10	50
		Taken T		76125-0900-01	1	10
G 1 1	0 :6.1	J1561 - Injection, immune globulin, (Gamunex-C/		76125-0900-25	2.5	25
Gammaked 10%	Grifols Therapeutics	Gammaked), non-	500 mg	76125-0900-50	5	50
1070	Therapeutics	lyophilized (e.g., liquid), 500		76125-0900-10	10	100
		mg		76125-0900-20	20	200
				13533-0800-12	1	10
		J1561 — Injection, immune		13533-0800-15	2.5	25
Gamunex-C	Grifols	globulin, (Gamunex-	500 m a	13533-0800-20	5	50
10%	Therapeutics	C/Gammaked), non- lyophilized (e.g., liquid), 500	500 mg	13533-0800-71	10	100
		mg		13533-0800-24	20	200
				13533-0800-40	40	400
		J1569 — Injection, immune		00944-2700-02	1	10
				00944-2700-03	2.5	25
Gammagard	Baxalta US	globulin, (Gammagard liquid), non-lyophilized,	500 mg	00944-2700-04	5	50
Liquid 10%	d 10% Inc.	(e.g., liquid), 500 mg	_	00944-2700-05	10	100
				00944-2700-06	20	200
				00944-2700-07	30	300
HyQvia 10%				00944-2510-02	2.5	25
(with		J1575 — Injection, immune		00944-2511-02	5	50
Recombinant	Baxalta US	globulin/ hyaluronidase,	100 mg	00944-2512-02	10	100
Human	Inc.	(Hyqvia), 100 mg immune globulin		00944-2513-02	20	200
Hyaluronidase 160 U/mL)				00944-2514-02	30	300
				00944-2850-01	1	5
	D 1 HG			00944-2850-03	2	10
Cuvitru 20%	Baxalta US	J1555 – Injection, immune globulin (Cuvitru), 100 mg	100 mg	00944-2850-05	4	20
	Inc.	globuliii (Cuviti u), 100 ilig		00944-2850-07	8	40
				00944-2850-09	10	50
				00069-1061-01	1	6
				00069-1802-01	1.65	10
Cutaquig	Octophorma	J1551 – Injection, immune globulin (cutaquig), 100 mg	100 mg	00069-1476-01	2	12
16.5%	Octapharma	giobuin (cutaquig), 100 mg	100 mg	00069-1960-01	3.3	20
				00069-1509-01	4	24
				00069-1965-01	8	48

SCIG: Hizentra, Gammagard Liquid, Gamunex-C, Gammaked, HyQvia, Cuvitru, Cutaquig, Xembify Prior Auth Criteria



Drug Name*	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
				13533-0810-05	1	5
Xembify 20% Grifols	J1558 — Injection, immune	100 mg	13533-0810-10	2	10	
	Ginois	globulin (Xembify), 100 mg	100 mg	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

- 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 v 2 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
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



ICD-10	ICD-10 Description	
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					
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)			



Medicare Part B Administrative Contractor (MAC) Jurisdictions				
Jurisdiction Applicable State/US Territory		Contractor		
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		

