



SCIG (immune globulin SC): Hizentra®, Gammagard Liquid®, 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

Scope: Medicaid*, Commercial, Medicare-Medicaid Plan (MMP)

*(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.

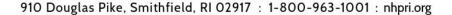
II. Dosing Limits

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	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 (PID)
	1840 (CIDP)
Gamunex-C, Gammaked,	336
Gammagard liquid	336
HyQvia	1200
Cuvitru & Cutaquig	1600
Xembify	1680





III. Summary of Evidence

Subcutaneous Immunoglobulin (SCIG) is indicated for the treatment of primary humoral immunodeficiency (PI). Prospective, open-label, single-arm, multi-center clinical studies have been conducted to determine the efficacy of subcutaneous infusion of IVIG in subjects with PI. The annual rate of serious bacterial infections (SBIs) was the primary endpoint across the clinical studies. The results of the clinical trials conducted on SCIQ are as follows: the annual rate of acute serious bacterial infections while on Gammagard Liquid subcutaneous treatment was 0.067, with an upper 99% confidence limit of 0.133, which is lower than the minimal goal of achieving a rate of <1 bacterial infection per patient-year. No subjects experienced an SBI in the study conducted on Hizentra (upper 99% confidence limit: 0.132). The rate of serious bacterial infections (SBIs) was 0.05 events per subject-year (1 event in 20 subject-years) (upper 99% confidence limit: 0.11) during Xembify treatment. The most common adverse reactions observed are local infusion site reactions, headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, upper respiratory tract infection, rash, pruritus, vomiting, abdominal pain (upper), migraine, arthralgia, pain, fall and nasopharyngitis.

IV. Initial Approval Criteria

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 patient must have failure or intolerance to the following preferred formulations: Gammaked/Gamunex-C or Gammagard liquid (for patients 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, ataxiatelangiectasia, 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 <u>both</u> of the following
 - o 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 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] †

- 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
 - O 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)

- Patient's disease course is progressive or relapsing and remitting for 2 months or longer; AND
- Patient has abnormal or absent deep tendon reflexes in upper or lower limbs; AND
- Electrodiagnostic testing indicating demyelination:
 - O 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**
 - O 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
 - o Reduced conduction velocity in at least 2 motor nerves; **OR**
 - o Prolonged distal motor latency in at least 2 motor nerves; **OR**
 - O Absent F wave in at least two motor nerves plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
 - o Prolonged F wave latency in at least 2 motor nerves; AND
- Patient 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)

V. Renewal Criteria

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

- Patient 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
 - o Decrease in the severity of infection

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

- 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
 - O Patient improved and stabilized on IVIG treatment: AND
 - o Patient was NOT receiving maximum dosing of Hizentra or Hyqvia prior to relapse

VI. 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/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 5 gram increment in adult patients)

Dosing formulas

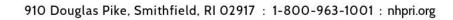
 $BMI = 703 \text{ x (weight in pounds/height in inches}^2)$

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.





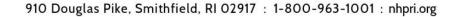
Indication	Dose		
ndication	Hizentra: Initiate therapy 1 w The recommended or 2 sessions over 1 If CIDP symptoms administered in 2 set of the series of the	or 2 consecutive days. worsen, consider increasing the essions over 1 or 2 consecutive worsen on the 0.4 g/kg body ediscontinuing Hizentra. In stable doses of IVIG prior to erapy with Hyqvia, calculate the elaw: previous IVIG dose (g)/n and dosing frequency of Hyqvianterval range in the clinical tri	weight per week dose, consider re-initiating thera
Chronic Inflammatory Demyelinating Polyneuropathy (CIPD)	while maintaining the Administer the calc week after the first	he same monthly equivalent Ig ulated one-week dose (1st infu Hyqvia dose, administer anoth can take up to 9 weeks, depend	gG dose. Ission) 2 weeks after the last IVGIGV infusion. One weekly equivalent dose (2nd infusion). Is amp-up schedule Dose Interval Not applicable 1-week-doseDose in Grams X 0.67 1-week-doseTotal Dose in Grams 2-week-doseTotal Dose in Grams
Inflammatory Demyelinating Polyneuropathy	while maintaining the Administer the calc week after the first A ramp-up period of below) Week* 1 2 3 4	he same monthly equivalent Igulated one-week dose (1st infu Hyqvia dose, administer another can take up to 9 weeks, dependent HyQvia Dose Ra Infusion Number No infusion 1st infusion 2nd infusion 3rd infusion	gG dose. Ission) 2 weeks after the last IVGIGV infusion. One weekly equivalent dose (2nd infusion). Ising on the dosing interval and tolerability (see table to be applied to be appli
Inflammatory Demyelinating Polyneuropathy	while maintaining the Administer the calc week after the first A ramp-up period of below) Week* 1 2 3 4 5	he same monthly equivalent Ig ulated one-week dose (1st infu Hyqvia dose, administer anoth can take up to 9 weeks, depend HyQvia Dose Ra Infusion Number No infusion 1st infusion 2nd infusion 3rd infusion No infusion	Amp-up Schedule Dose Interval Not applicable 1-week-doseTotal Dose in Grams Not applicable 2-week-doseTotal Dose in Grams Not applicable Not applicable
Inflammatory Demyelinating Polyneuropathy	while maintaining the Administer the calc week after the first A ramp-up period of below) Week* 1 2 3 4 5 6	he same monthly equivalent Igulated one-week dose (1st infu Hyqvia dose, administer another take up to 9 weeks, dependent of the Infusion Number No infusion 1st infusion 2nd infusion 3rd infusion No infusion 4th infusion	gG dose. Ission) 2 weeks after the last IVGIGV infusion. One weekly equivalent dose (2nd infusion). Ising on the dosing interval and tolerability (see table amp-up Schedule Dose Interval Not applicable 1-week-doseDose in Grams X 0.67 1-week-doseTotal Dose in Grams 2-week-doseTotal Dose in Grams Not applicable 3-week-dose

Indication	Dose			
	• Switchin	Weekly dose: 1.37*(pro May be administered f Biweekly dose: twice the Frequent dosing (2-7 to of times per week and from SCIG Initiate therapy 1 week Weekly dose (in grams Biweekly dose: multiple	after the last SCIG dose) should be same as the weekly do y the prior weekly dose by 2	biweekly)
Primary immune deficiency (PID)	 Switching HyQvia: Naïve to (see table) Switching 	dose(g)/number of we o IgG or switching from below)	a after the last IVIG doseWeekly deeks between IVIG doses) SCIG: 300 to 600 mg/kg at 3 to 4	lose: 1.37*(previous IVIG 4 week intervals after initial ramp-up evious IV treatment after initial ramp-
	- T (*****		Treatment Interval/Dosage Ra	ump-up Schedule
	Week	Infusion Number	3-week treatment interval	4-week treatment interval
	1	1 st infusion	Dose in Grams X 0.33	Dose in Grams X 0.25
	2	2 nd infusion	Dose in Grams X 0.67	Dose in Grams X 0.50
	4	3 rd infusion	Total Dose in Grams	Dose in Grams X 0.75
	7	4 th infusion	Total Dose in Grams	Total Dose in Grams
	Xembify: Switchin	Weekly dose: 1.37*(proweeks between IVIG	eek after the last IVIG infusion. evious monthly (or every 3- week) doses) ne dose in grams to mL, multiply t	,



Indication	Dose
Indication	Dose
	 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)
	Cuvitru:
	Switching from IVIG or HyQvia:
	Initiate therapy 1 week after the last IVIG dose
	o midate dictapy i week after the last IVIO 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)
	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)
	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 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)
	o May be administered from daily up to every two weeks (biweekly)
	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)
	 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.





VII. Billing Code/Availability Information

HCPCS code & NDC:

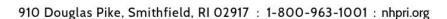
Drug Name	Manufacturer	HCPCS Code or CPT Code	1 Billable unit	NDC	IgG (grams) per SDV	Volume (mL)
				44206-0451-01	1	5
11: 200/	CSL Behring	J1559 — Injection, immune globulin (Hizentra), 100 mg	100	44206-0452-02	2	10
Hizentra 20%	AG	giobulii (1 lizentia), 100 mg	100 mg	44206-0454-04	4	20
				44206-0455-10	10	50
		74574		76125-0900-01	1	10
	17. 1.	J1561 Injection, immune globulin, (Gamunex-		76125-0900-25	2.5	25
Gammaked 10%	Kedrion Biopharma, Inc.	C/Gammaked), non-	500 mg	76125-0900-50	5	50
	Бюрпанна, піс.	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 10%	Grifols	globulin, (Gamunex-	E00 mag	13533-0800-20	5	50
Gamunex-C 1076	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
				00944-2700-02	1	10
	-	J1569 — Injection, immune		00944-2700-03	2.5	25
Gammagard Liquid	Baxter Healthcare	globulin, (Gammagard liquid), non-lyophilized, (e.g. liquid), 500 mg	500 mg	00944-2700-04	5	50
10%	Corporation		-	00944-2700-05	10	100
	Gorporadon			00944-2700-06	20	200
				00944-2700-07	30	300
				00944-2510-02	2.5	25
HyQvia 10% (with	Baxter	J1575 — Injection, immune		00944-2511-02	5	50
Recombinant Human Hyaluronidase 160	Healthcare	globulin/hyaluronidase, (Hyqvia), 100 mg immune	100 mg	00944-2512-02	10	100
U/mL)	Corporation	globulin		00944-2513-02	20	200
				00944-2514-02	30	300
				00944-2850-01	1	5
Cuvitru 20%	Baxalta US Inc.	J1555 – Injection, immune	100 mg	00944-2850-03	2	10
Cuvittu 2070	Daxaita US IIIC.	globulin (Cuvitru), 100 mg	100 mg	00944-2850-05	4	20
				00944-2850-07	8	40
Cutaquig 16.5%	Octapharma	J1551	N/A	68892-0810-01	1	6



Drug Name	Manufacturer	HCPCS Code or CPT Code	1 Billable unit	NDC	IgG (grams) per SDV	Volume (mL)
				68892-0810-02	1.65	10
				68892-0810-03	2	12
				68892-0810-04	3.3	20
				68892-0810-05	4	24
				68892-0810-06	8	48
	Grifols	90284; J1558		13533-0810-05	1	5
Xembify 20%			N/A	13533-0810-10	2	10
Acmony 2070	Ginois			13533-0810-20	4	20
				13533-0810-50	10	50
Immune Globulin, Human,	N/A	J3590 – unclassified biologic; C9399 – unclassified drug or biological	N/A	N/A	N/A	N/A
Subcutaneous		90284 – immune globulin (SCIg), human, for use in subcutaneous infusions				

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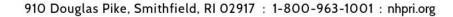




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Appendix 1 – Covered Diagnosis Codes

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	



ICD-10	ICD-10 Description
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 preced	The preceding information is intended for non-Medicare coverage determinations.			
Jurisdiction	NCD/LCA/LCD Contractor Document (s)			
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			



	Medicare Part B Administrative Contractor (MAC) Jurisdictions			
Jurisdiction	Applicable State/US Territory Contractor			
, ,	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	КҮ, ОН	CGS Administrators, LLC		

Policy Rationale:

Hizentra, Gammagard Liquid, 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 INTEGRITY (Medicare-Medicaid Plan) 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.