PHARMACY PRE-AUTHORIZATION CRITERIA

ConnectiCare

DRUG (S)	**SCIG: Hizentra®, Gammagard Liquid®, Gamunex®-C, Gammaked®, Hyqvia, Cuvitru, Xembify (immune globulin SQ)**
POLICY #	
INDICATIONS	Subcutaneous Immune Globulins are FDA-Approved for the following indications: • **Primary immunodeficiency (PID)/Wiskott -Aldrich syndrome** • **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**
CRITERIA	**Initial approval criteria:** SCIG may be considered medically necessary if one of the below conditions are met **AND** use is consistent with the medical necessity criteria that follows: • The first dose may be given at the facility of choice by the physician; all subsequent doses will be given by home infusion coordinated by ConnectiCare's preferred vendors • ConnectiCare's preferred site of care for this medication is home infusion. Clinical rationale and documentation must be provided for review for exceptions. The following are considerations for services outside the home: o Documented history of a severe reaction to this medication or any constituent of it. o Severe reaction is defined as anaphylactic reaction. o The patient should have a history of reactions and not be based on the potential of the medication to induce such reactions. o Documented intolerance to this medication requiring constant telemetry monitoring of vitals. o Unsafe home environment. o No access to 911 services. o Documented presence of IGA auto antibodies. **Coverage is provided in the following conditions:** • Baseline values for BUN and serum creatinine obtained within 30 days of request; **AND** **Primary immunodeficiency (PID)/Wiskott - Aldrich syndrome †** Such as: 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)

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[**list not all inclusive**]

- For HyQvia ONLY: Patient must be ≥ 18 years old,
- For Gammaked, Hizentra Xembify, Cuvitru, Gamunex-C, and Gammagard Liquid: Patient must be ≥ 2 years old ; **AND**
- Patient's IgG level is <200 **OR** **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 or deep skin abscesses
    - 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

† FDA Approved Indication(s)

OR

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- For Gammaked, Hizentra, and Gamunex C : Patient must be ≥ 18 years old; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **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)

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Renewal Criteria:

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

- Patient continues to meet criteria identified above; **AND**
- Absence of unacceptable toxicity from the drug; **AND**
- BUN and serum creatinine obtained within the last 6 months and the concentration and rate of infusion adjusted accordingly; **AND**

Primary immunodeficiency (PID)/Wiskott-Aldrich syndrome

- 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)

- 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.

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DOSAGE/ADMIN	

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
Primary immune deficiency including Wiskott-Aldrich Syndrome	<u>Hizentra:</u> ▪ Weekly dose: 1.37*(previous IVIG dose(g)/number of weeks between IVIG doses) ▪ Biweekly dose: twice the weekly dose (using calculation above)
	<u>Gamunex-C/Gammaked/Gammagard Liquid:</u> ▪ 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

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	after initial ramp-up* ▪ Switching from IGIV: use the same dose and frequency as the previous IV treatment after initial ramp-up*
	<u>Cuvitru:</u> ▪ Switching from IVIG or HyQvia: o Weekly dose: 1.30*(previous IVIG or HyQvia dose (g)/number of weeks between IVIG or HyQvia doses) o May be administered from daily up to every two weeks (biweekly) o 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) 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

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.

*HyQvia initial treatment interval/dosage ramp-up schedule

Week	Infusion Number	3-week treatment interval	4-week treatment interval
1	1st infusion	Dose in Grams X 0.33	Dose in Grams X 0.25
2	2nd infusion	Dose in Grams X 0.67	Dose in Grams X 0.50
4	3rd infusion	Total Dose in Grams	Dose in Grams X 0.75
7	4th infusion	N/A	Total Dose in Grams

LIMITATIONS

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

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

Drug Name	Dose/ week	Dose/28 days
Hizentra	24 g	96 g
Gamunex-C & Gammaked	24 g	96 g
Gammagard liquid	24 g	96 g

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HyQvia	17.5 g	69 g
Cuvitru	23 g	92 g

B. Max Units (per dose and over time) [Medical Benefit]:

Drug Name	Billable units/28 days
Hizentra	960
Gamunex-C & Gammaked	192
Gammagard liquid	192
HyQvia	690
Cuvitru (J3590)	920
Cuvitru (90284)	920
Xembify	N/A (96 gm)

***Xembify** -Prior to switching to Xembify, obtain patient's serum IgG trough level to guide subsequent dose adjustment. Switching from immune globulin intravenous (human), 10% (IVIG) to XEMBIFY: calculate the dose by using a dose adjustment factor. Xembify is to be given one week after the last IVIG infusion.

Billing Code/Availability Information

J-Code & NDC:

Drug Name	Manufacturer	J Code	1 Billable unit	NDC	IgG (grams)	Volume (mL)
Hizentra 20%	CSL Behring AG	J1559 – Injection, immune globulin (Hizentra), 100 mg	100 mg	44206-0451-01	1	5
				44206-0451-02	2	10
				44206-0451-04	4	20
				44206-0451-10	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	Grifols	J1561 – Injection,	500 mg	13533-0800-12	1	10

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10%	Therapeutics	immune globulin, (Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg		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%	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.	J3590 – unclassified biologic	N/A	00944-2850-01	1	5
				00944-2850-03	2	10
		90284 – immune globulin (SCIg), human, for use in subcutaneous infusions	100 mg	00944-2850-05	4	20
				00944-2850-07	8	40
Xembify	GRIFOLS USA	J3590 – unclassified biologic	N/A	13533-0810-05	1	5
				13533-0810-06	1	5
				13533-0810-10	2	10
				13533-0810-11	2	10
				13533-0810-20	4	20
				13533-0810-21	4	20
				13533-0810-50	10	50
				13533-0810-51	10	50

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REFERENCES	1. Hizentra [package insert]. Bern, Switzerland; CSL Behring AG; October 2016. Accessed August 2017. 2. HyQvia [package insert]. Westlake Village, CA; Baxter Healthcare Corporation; September 2016. Accessed August 2017. 3. Cuvitru [package insert]. Westlake Village, CA; Baxalta US Inc.; September 2016. Accessed August 2017. 4. Gammagard Liquid [package insert]. Westlake Village, CA; Baxter Healthcare Corporation; June 2016. Accessed August 2017. 5. Gamunex®-C [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc.; September 2016. Accessed August 2017. 6. Gammaked™ [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc.; September 2016. Accessed August 2017. 7. Jeffrey Modell Foundation Medical Advisory Board, 2013. 10 Warning Signs of Primary Immunodeficiency. Jeffrey Modell Foundation, New York, NY 8. 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. 9. 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). 10. 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. 11. Emerson GG, Herndon CN, Sreih AG. Thrombotic complications after intravenous immunoglobulin therapy in two patients. Pharmacotherapy. 2002;22:1638-1641. 12. Department of Health (London). Clinical Guidelines for Immunoglobulin Use: Update to Second Edition. August, 2011. 13. Provan, Drew, et al. "Clinical guidelines for immunoglobulin use." Department of Health Publication, London (2008). 14. Dantal J. Intravenous Immunoglobulins: In-Depth Review of Excipients and Acute Kidney Injury Risk. Am J Nephrol 2013;38:275-284. 15. 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.

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16. First Coast Service Options, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (L34007). Centers for Medicare & Medicaid Services, Inc. Updated on 1/3/2017 with effective date 1/17/2017. Accessed August 2017.
17. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Immune Globulins (L34771). Centers for Medicare & Medicaid Services, Inc. Updated on 6/20/2017 with effective date 7/1/2017. Accessed August 2017.
18. XEMBIFY(R) subcutaneous injection, immune globulin human-klhw subcutaneous injection. Grifols Therapeutics LLC (per FDA), Research Triangle Park, NC, 2019.

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

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APPENDIX 2

Centers for Medicare and Medicaid Services (CMS)

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 Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): N	**NCD/LCD/Article Document (s):** L34007
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34007&bc=gAAAAAAAAAAAAA==	
Jurisdiction(s): 5,8	**NCD/LCD/Article Document (s):** L34771
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L34771&bc=gAAAAAAAAAAAAA==	

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	Cahaba Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes	Novitas Solutions, Inc.

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	<table><tr><td></td><td>Arlington & Fairfax counties and the city of Alexandria in VA)</td><td></td></tr><tr><td>K (13 & 14)</td><td>NY, CT, MA, RI, VT, ME, NH</td><td>National Government Services, Inc. (NGS)</td></tr><tr><td>15</td><td>KY, OH</td><td>CGS Administrators, LLC</td></tr></table>
P&T REVIEW HISTORY	11/2017, 5/18, 7/18
REVISION RECORD	5/18, 1/20- added Xembify