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

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 12 months thereafter.

II. Dosing Limits

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

Drug Name	Billable units/28 days
Hizentra	1840 (CIDP) 1680 (All other indications)
Gamunex-C, Gammaked, & Gammagard liquid/ERC	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 (All other indications)	Week 1: 300 Week 2: 600 Week 4: 900	1200
Xembify	180 daily for 5 days	1680

III. Initial Approval Criteria [1-9,13,16,19]

Coverage is provided in the following conditions:

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

Primary Immunodeficiency (PID) † [1-9, 12,13,19,36]

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 [3,4,22,37]

- 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)
- ***§** Refer to the IVIG (immune globulin IV) medical necessity criteria (Document Number: IC-0071) for the relevant intravenous criteria requirements*

Acquired Immune Deficiency Secondary to Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) ‡ [32,33,36]

- 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

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

IV. Renewal Criteria [1-9,16,19,32,33]

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)

- 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 [1-9,14-16,32-35]

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

<table>
<tr><th>Indication</th><th>Dose ❖</th></tr>
<tr><td></td><td>
<table>
<tr><td>5</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>6</td><td>4th infusion</td><td>3-week-dose</td></tr>
<tr><td>7</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>8</td><td>No infusion</td><td>Not applicable</td></tr>
<tr><td>9</td><td>5th infusion</td><td>4-week-dose</td></tr>
</table>
*Clock starts one week after the last IVIG 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/Gammagard Liquid ERC:</u>

Switching from IVIG

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

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

Indication	Dose ❖
	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*

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	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 grams/number of weeks between IVIG doses]
  - 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
- 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
- Treatment naïve
  - 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
  - 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)

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

Drug Name	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
				44206-0458-24	4	20
				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 ERC	Takeda Pharmaceuticals U.S.A., Inc.	J3590 – unclassified biologics	N/A	00944-2705-50	5	50
				00944-2705-10	10	100
Gammagard Liquid 10%*	Takeda Pharmaceuticals U.S.A., 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)	Takeda Pharmaceuticals U.S.A., 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%*	Takeda Pharmaceuticals U.S.A., 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
Cutaquig 16.5%*	Octapharma	J1551 – Injection, immune globulin (cutaquig), 100 mg	100 mg	00069-1061-01	1	6
				00069-1802-01	1.65	10
				00069-1476-01	2	12

Drug Name	Manufacturer	HCPCS Code	1 Billable unit	NDC	IgG (grams) per vial/syringe	Volume (mL)
				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, 100 mg, each*

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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

ICD-10	ICD-10 Description
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 (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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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