Medical Policy:

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

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.107	March 6, 2025	November 1, 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

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

Dosing Limits [Medical Benefit]

A. Max Units (per dose and over time):

Drug Name	Billable units/ per 21 or 28 days
Hizentra	1680 (PID)
	1840 (CIDP)
Gamunex-C & Gammaked	336
Gammagard liquid	336
HyQvia	1600 (CIDP) 1200 (PID)
Cutaquiq	1600

Cuvitru	1600
Xembify	1680

***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.

Guideline

I. Initial Approval Criteria

- Coverage is provided in the following conditions:

1. **Primary immunodeficiencies (PI) †**

   Such as: x-linked agammaglobulinemia, Wiskott -Aldrich syndrome, 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**]

   A. For Gammagard Liquid, Gamunex-C, Gammaked, Hizentra, HyQvia, Cutaquig, Cuvitru, Xembify: Patient must be ≥ 2 years old;

      AND

   B. Patient's IgG level is <200 mg/dL **OR both** of the following

      i. Patient has a history of multiple hard to treat infections as indicated by at least **one** of the following:

         a. Four or more ear infections within 1 year
         b. Two or more serious sinus infections within 1 year
         c. Two or more months of antibiotics with little effect
         d. Two or more pneumonias within 1 year
         e. Recurrent or deep skin abscesses
         f. Persistent thrush in the mouth or fungal infection on the skin
         g. Need for intravenous antibiotics to clear infections
         h. Two or more deep-seated infections including septicemia
         i. Family history of PID**; AND**

      ii. The patient has a deficiency in producing antibodies in response to vaccination; **AND**

         a. Titers were drawn before challenging with vaccination; **AND**
         b. Titers were drawn between 4 and 8 weeks of vaccination

2. **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and HyQvia ONLY] †**

   A. Patient must be ≥ 18 years old; **AND**

   B. Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**

      i. Used as initial maintenance therapy for prevention of disease relapses after treatment and stabilization with intravenous immunoglobulin (IVIG)§; **OR**

      ii. Used for re-initiation of maintenance therapy after experiencing a relapse and requiring re-induction therapy with IVIG (see Hizentra/HyQvia Renewal 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:**
  - 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
  - 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
  - Reduced conduction velocity in at least 2 motor nerves; OR
  - Prolonged distal motor latency in at least 2 motor nerves; OR
  - Absent F wave in at least two motor nerves plus one other demyelination criterion listed here in at least 1 other nerve; OR
  - Prolonged F wave latency in at least 2 motor nerves; AND
- **Cerebrospinal fluid analysis indicates the following:**
  - CSF white cell count of <10 cells/mm^3; AND
  - CSF protein is elevated; 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)

II. Renewal Criteria

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

- Patient continues to meet the indication-specific relevant criteria identified in Initial Criteria; **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**

1. **<u>Primary immunodeficiencies (PI)</u>**
   A. Disease response as evidenced by one or more of the following:
      i. Decrease in the frequency of infection
      ii. Decrease in the severity of infection

2. **<u>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and HyQvia ONLY]</u>**
      A. Renewals will be authorized for patients who have demonstrated a beneficial clinical response to maintenance therapy with subcutaneous immune globulin 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**

3. **<u>Renewals for re-initiation of Hizentra and HyQvia (for the treatment of CIPD) only:</u>**
   A. Patient is re-initiating maintenance therapy; **AND**
   B. Patient has improved and stabilized on IVIG treatment before re-initiating Hizentra; **AND**
   C. Patient was NOT receiving maximum dosing of Hizentra or HyQvia prior to relapse

Limitations/Exclusions

SCIG: Hizentra, Gammagard Liquid, Gamunex-C, Gammaked, HyQvia, Cutaquiq, Cuvitru, Xembify are considered investigational when used for any indication not listed above.

Applicable Procedure Codes

Code	Description
J1551	Injection, immune globulin (cutaquig), 100 mg
J1559	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin, (Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), non-lyophilized, (e.g. liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase, (HyQvia), 100 mg immune globulin
J1555	Injection, immune globulin (Cuvitru), 100 mg
J1558	Injection, immune globulin, 100 mg (Xembify). J-Code effective date: 07/01/2020
J3590	Unclassified biologics
90284	Immune globulin (SCIg), human, for use in subcutaneous infusions

Applicable NDCs

Drug Name	NDC	IgG (grams)	Volume (mL)
Hizentra 20%	44206-0451-01	1	5
	44206-0452-02	2	10
	44206-0454-04	4	20
	44206-0455-10	10	50
Hizentra 20% (Prefilled Syringes)	44206-0456-21	1	5
	44206-0457-22	2	10
	44206-0458-24	4	20
	44206-0455-25	10	50
Gammaked 10%	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%	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%	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)	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%	00944-2850-01	1	5
	00944-2850-03	2	10
	00944-2850-05	4	20
	00944-2850-07	8	40
Cutaquig 16.5%	00069-1061-01	1	6
	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	13533-0810-05	1	5
	13533-0810-10	2	10
	13533-0810-20	4	20
	13533-0810-50	10	50

ICD-10 Diagnoses

Code	Description
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.11	Chronic lymphocytic leukemia of B-cell type in 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
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 Hizentra and Hyqvia ONLY
G61.89	Other inflammatory polyneuropathies Hizentra and Hyqvia ONLY
G62.89	Other specified polyneuropathies Hizentra and Hyqvia ONLY

Revision History

<table>
<tr><th>Company(ies)</th><th>DATE</th><th>REVISION</th></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>03/06/2025</td><td>Update: Updated dosing limits, NDCs: Initial Criteria: Primary immunodeficiencies (PI) † added: “Persistent thrush in the mouth or fungal infection on the skin and Family history of PID” as options. Added HyQvia to: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and HyQvia ONLY] †

Renewal Criteria: added: “Patient continues to meet the indication-specific relevant criteria identified in Initial Criteria; AND 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
Added HyQvia to “Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra and HyQvia ONLY]” renewal criteria. Added: “without relapses, based on an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.);” to the following statement: “Renewals will be authorized for patients who have demonstrated a beneficial clinical response to maintenance therapy with subcutaneous immune globulin 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”
Added HyQvia to: “Renewals for re-initiation of Hizentra and HyQvia (for the treatment of CIPD) only:”
Added: “Patient was NOT receiving maximum dosing of Hizentra or HyQvia prior to relapse”</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>11/25/2024</td><td>Added Cutaquig to policy and criteria.
Removed: “For HyQvia ONLY: Patient must be ≥ 18 years old; “
Added HyQvia to line “For Gammagard Liquid, Gamunex-C, Gammaked, Hizentra, HyQvia, Cutaquig, Cuvitru, Xembify: Patient must be ≥ 2 years old”
Removed code: B20
Added codes: J1551
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<tr><td>C91.10</td><td>Chronic lymphocytic leukemia of B-cell type not having achieved remission</td></tr>
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EmblemHealth & ConnectiCare	4/27/2023	Annual Review: no criteria changes
EmblemHealth & ConnectiCare	1/13/2023	Transfer to New Template
EmblemHealth & ConnectiCare	2/14/2022	Removed PANDAS/PANS coverage as per Massachusetts DOI Bulletin 2021-06 for Massachusetts residents under the Commercial line of business, starting 1/1/2022
EmblemHealth & ConnectiCare	2/14/2022	Removed BUN/SCr Requirements from Initial and renewal Criteria
EmblemHealth & ConnectiCare	1/18/2022	Updated Primary immunodeficiency (PID)/Wiskott -Aldrich syndrome indication to Primary immunodeficiencies (PI) and moved Wiskott-Aldrich below as an example for clarification Added coverage of Hizentra to Primary immunodeficiencies to capture FDA approval
EmblemHealth & ConnectiCare	11/29/2021	Added PANDAS/PANS coverage as per Massachusetts DOI Bulletin 2021-06 for Massachusetts residents under the Commercial line of business, starting 1/1/2022
EmblemHealth & ConnectiCare	2/1/2021	Removed the following from Renewal Criteria: • "Patient continues to meet criteria identified in section III; " Clarified Hizentra renewal criteria.
EmblemHealth & ConnectiCare	06/10/2020	Added J-Code (J1558): Injection, immune globulin, 100 mg (Xembify). J-Code effective date: 07/01/2020
EmblemHealth & ConnectiCare	11/01/2019	-Added Xembify to this MP, included drug in title -Added under Dosing Limits: 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. - Xembify NDC's, Pkg sizes and Gm strength added to chart -Updated age restrictions for PID indication for Gammagard Liquid, Gamunex-C, Gammaked, HyQvia, Cuvitru, Xembify

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