Medical Policy:

Besponsa® (inotuzumab ozogamicin) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.47	April 1, 2024	

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.

Definitions

Besponsa (inotuzumab ozogamicin) is a humanized CD22-directed monoclonal antibody-drug conjugate which is composed of the IgG4 kappa antibody inotuzumab (which is specific for human CD22), a calicheamicin component (a cytotoxic agent that causes double-stranded DNA breaks), and an acid-cleavable linker that covalently binds the calicheamicin to inotuzumab. After the antibody-drug conjugate binds to CD22, the CD22-conjugate complex is internalized, and releases calicheamicin. Calicheamicin binds to the minor groove of DNA to induce double strand cleavage and subsequent cell cycle arrest and apoptosis.

Besponsa (inotuzumab ozogamicin) is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Length of Authorization

Coverage will be provided for 6 months (for up to a maximum of 6 cycles) and may not be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Cycle 1: 27 billable units on Day 1, 18 billable units on Day 8 and Day 15 of a 21 to 28-day cycle
Subsequent Cycles (maximum of 5 cycles)

- 27 billable units on Day 1, 18 billable units on Day 8 and Day 15 of a 28-day cycle for up to 2 cycles
- 18 billable units on Day 1, Day 8, and Day 15 of a 28-day cycle for up to 3 cycles

Guideline

Besponsa (inotuzumab ozogamicin) may be considered medically necessary for the following diagnoses when subsequent criteria are met:

I. INITIAL CRITERIA

1. **Adult B-cell precursor acute lymphoblastic leukemia (ALL):**
   - A. Patient is 18 years of age or older; **AND**
   - B. Patient has CD22-positive disease; **AND**
   - C. Patient has relapsed or refractory disease; **AND**
   - D. Used as single agent therapy; **OR**
   - E. Used in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine); **AND**
     - i. Patient is Philadelphia chromosome (Ph)-negative; **OR**
     - ii. Patient is Philadelphia chromosome (Ph)-positive and refractory to prior tyrosine kinase inhibitor therapy *(e.g., imatinib, dasatinib, ponatinib,nilotinib, bosutinib, etc.);* **OR**
   - F. Used in combination with tyrosine kinase inhibitor (TKI) therapy *(e.g., bosutinib, dasatinib, imatinib, nilotinib, or ponatinib)*; **AND**
     - i. Patient is Philadelphia chromosome (Ph)-positive; **OR**
   - G. Used as induction therapy in patients ≥65 years of age or with substantial comorbidities; **AND**
     - i. Used in combination with mini-hyper CVD; **AND**
     - ii. Patient is Philadelphia chromosome (Ph)-negative

2. **Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia (ALL)**
   - A. Patient is at least 1 year of age; **AND**
   - B. Patient has relapsed or refractory disease**; AND**
   - C. Used as single agent therapy; **AND**
     - i. Patient is Philadelphia chromosome (Ph)-negative**; OR**
     - ii. Patient is Philadelphia chromosome (Ph)-positive**; AND**
       - a. Patient is intolerant or refractory to prior tyrosine kinase inhibitor (TKI) therapy *(e.g. imatinib, dasatinib etc.)*

Limitations/Exclusions

1. Approval will be granted for 6 months, and **may not be renewed**

Applicable Procedure Codes

Code	Description
J9229	Injection, inotuzumab ozogamicin, 0.1 mg

Applicable NDCs

Code	Description

00008-0100-01	Besponsa 0.9mg Solution Reconstituted J9229 Injection, inotuzumab ozogamicin, 0.1 mg

ICD-10 Diagnoses

Code	Description
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ site
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse

Revision History

<table>
<tr><th>Company(ies)</th><th>DATE</th><th>REVISION</th></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>4/1/2024</td><td>Annual Review: Added Pediatric ALL indication and criteria</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>7/25/2023</td><td>Annual Review:
<u>B-cell precursor acute lymphoblastic leukemia (ALL):</u> Initial Criteria:
Removed wording “Besponsa will be used as single agent therapy; AND
iii. Patient is Philadelphia chromosome (Ph)-negative; OR
iv. Patient is Philadelphia chromosome (Ph)-positive and failed previous therapy with a tyrosine kinase inhibitor; AND
H. Besponsa will be used as single agent therapy.”
Added ” Used as single agent therapy; OR
I. Used in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine); AND
i. Patient is Philadelphia chromosome (Ph)-negative; OR
ii. Patient is Philadelphia chromosome (Ph)-positive and refractory to prior tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, ponatinib,nilotinib, bosutinib, etc.); OR
J. Used in combination with tyrosine kinase inhibitor (TKI) therapy (e.g., bosutinib, dasatinib, imatinib, nilotinib, or ponatinib); AND
i. Patient is Philadelphia chromosome (Ph)-positive; OR
K. Used as induction therapy in patients ≥65 years of age or with substantial comorbidities; AND
i. Used in combination with mini-hyper CVD; AND
ii. Patient is Philadelphia chromosome (Ph)-negative”
Added ICD-10 Codes:
C83.50 Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51 Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck</td></tr>
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		C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
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		C83.57	Lymphoblastic (diffuse) lymphoma, spleen
		C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
		C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ site
EmblemHealth & ConnectiCare	4/04/2022	Transferred policy to new template	
EmblemHealth & ConnectiCare	12/30/2020	Annual review: no policy changes	
EmblemHealth & ConnectiCare	10/30/2019	Annual review	
EmblemHealth & ConnectiCare	12/3/2018	Added J9229 and removed C9028 from Applicable Procedure Codes.	

References

1. Besponsa [package insert]. Philadelphia, PA; Pfizer Inc., March 2018. Accessed October 2019.
2. Kantarjian HM, DeAngelo DJ, Stelljes M, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. N Engl J Med. 2016 Aug 25;375(8):740-53.
3. 3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) inotuzumab ozogamicin. National Comprehensive Cancer Network, 2017. 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 August 2017.