Besponsa® (inotuzumab ozogamicin)
(Intravenous)

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Document Number: IC-0453

Last Review Date: 05/02/2024
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I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Besponsa 0.9 mg powder for injection single-dose vial: 7 vials per 21 days

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

- 63 billable units every 21 days (for up to a maximum of 6 cycles)

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient has not previously received treatment with inotuzumab ozogamicin; **AND**

Universal Criteria [1-3]

- Patient has CD22-positive disease; **AND**
- Baseline electrocardiogram (ECG) is within normal limits prior to initiating therapy and will be periodically monitored during treatment; **AND**

Adult B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) † ‡ Φ [1-3,7e]

- Patient is at least 18 years of age; **AND**
  - Patient has relapsed or refractory disease; **AND**
    - Used as single agent therapy; **AND**
      - Patient is Philadelphia chromosome (Ph)-negative; **OR**
      - Patient is Philadelphia chromosome (Ph)-positive and refractory to prior tyrosine kinase inhibitor (TKI) therapy (e.g., imatinib, dasatinib, ponatinib, nilotinib, bosutinib, etc.); **OR**

- Used in combination with mini-hyper-CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine), with or without blinatumomab as consolidation*; **AND**
  - Patient is Philadelphia chromosome (Ph)-negative; **OR**
- Used in combination with TKI therapy (e.g., bosutinib, dasatinib, imatinib, nilotinib, or ponatinib); **AND**
  - Patient is Philadelphia chromosome (Ph)-positive; **OR**

o Used as frontline therapy; **AND**

- Patient is at least 60 years of age; **AND**
- Used in combination with mini-hyper-CVD, with or without blinatumomab as consolidation*; **AND**
- Patient is Philadelphia chromosome (Ph)-negative

***Note:** *May be used with rituximab for adults <65 years of age without substantial comorbidities.*

Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) † ‡ [3,4]

- Patient is at least 1 year of age; **AND**
- Patient has relapsed or refractory disease; **AND**
- Patient does not have a history of prior or ongoing hepatic sinusoidal obstruction syndrome (SOS); **AND**
- Used as single agent therapy

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

IV. Renewal Criteria [1]

Coverage may NOT be renewed.

V. Dosage/Administration [1]

Indication	Dose
B-Cell Precursor ALL	**Cycle 1:** • 1.8 mg/m^2 total per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2) • Cycle 1 is 3 weeks in duration, but may be extended to 4 weeks if the patient achieves CR or CRi, and/or to allow recovery from toxicity

	Subsequent Cycles (cycles are 4 weeks in duration): CR or CRi achieved • 1.5 mg/m^2 total per cycle, administered as 3 divided doses on Day 1 (0.5 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2) Did not achieve CR or CRi • 1.8 mg/m^2 total per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2) • Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment. **Patients proceeding to HSCT:** • Recommended duration of treatment is 2 cycles • A third cycle may be considered for those patients who do not achieve CR or CRi and MRD negativity after 2 cycles **Patients not proceeding to HSCT:** • Additional cycles of treatment, up to a maximum of 6 cycles, may be administered
CR (complete remission); CRi (complete remission with incomplete hematologic recovery); HSCT (hematopoietic stem cell transplant); MRD (minimal residual disease) • *CR is defined as < 5% blasts in the bone marrow and the absence of peripheral blood leukemic blasts, full recovery of peripheral blood counts (platelets ≥ 100 × 10^9/L and absolute neutrophil counts [ANC] ≥ 1 × 10^9/L) and resolution of any extramedullary disease.* • *CRi is defined as < 5% blasts in the bone marrow and the absence of peripheral blood leukemic blasts, incomplete recovery of peripheral blood counts (platelets < 100 × 10^9/L and/or ANC < 1 × 10^9/L) and resolution of any extramedullary disease.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9229 – Injection, inotuzumab ozogamicin, 0.1 mg: 1 billable unit = 0.1 mg

NDC:

- Besponsa 0.9 mg lyophilized powder in single-dose vial: 00008-0100-xx

VII. References (STANDARD)

1. Besponsa [package insert]. Philadelphia, PA; Pfizer Inc.; March 2024. Accessed April 2024.
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. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) inotuzumab ozogamicin. National Comprehensive Cancer Network, 2024. 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 April 2024.
4. Bhojwani D, Sposto R, Shah NN, et al. Inotuzumab ozogamicin in pediatric patients with relapsed/refractory acute lymphoblastic leukemia [published correction appears in Leukemia. 2019 Mar 7;:]. Leukemia. 2019;33(4):884–892.

5. O'Brien MM, Ji L, Shah NN, et al. Phase II trial of inotuzumab ozogamicin in children and adolescents with relapsed or refractory B-cell acute lymphoblastic leukemia: Children's Oncology Group Protocol AALL1621. J Clin Oncol 2022;40:956-967
6. Pennesi E, Michels N, Brivio E, et al. Inotuzumab ozogamicin as single agent in pediatric patients with relapsed and refractory acute lymphoblastic leukemia: results from a phase II trial. Leukemia 2022;36:1516-1524
7. Jabbour EJ, Sasaki K, Ravandi F, et al. Inotuzumab ozogamicin in combination with low-intensity chemotherapy (mini-HCVD) with or without blinatumomab versus intensive chemotherapy (HCVAD) as frontline therapy for older patients with Philadelphia chromosome-negative acute lymphoblastic leukemia: A propensity score analysis. Cancer 2019;125:2579-2586.

VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Acute Lymphoblastic Leukemia, Version 4.2023. National Comprehensive Cancer Network, 2024. 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 NCCN Guidelines, go online to NCCN.org. Accessed April 2024.

2e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Pediatric Acute Lymphoblastic Leukemia, Version 4.2024. National Comprehensive Cancer Network, 2024. 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 NCCN Guidelines, go online to NCCN.org. Accessed April 2024.

3e. Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Engl J Med 2017; 376:836-847.

4e. Martinelli G, Boissel N, Chevallier P, et al. Complete Hematologic and Molecular Response in Adult Patients With Relapsed/Refractory Philadelphia Chromosome-Positive B-Precursor Acute Lymphoblastic Leukemia Following Treatment With Blinatumomab: Results From a Phase II, Single-Arm, Multicenter Study. J Clin Oncol. 2017 Jun 1;35(16):1795-1802.

5e. Maude S, Laetsch T, Buechner J, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med 2018; 378:439-448.

6e. Jabbour E, Ravandi F, Kebriaei P, et al. Salvage Chemoimmunotherapy With Inotuzumab Ozogamicin Combined With Mini-Hyper-CVD for Patients With Relapsed or Refractory Philadelphia Chromosome-Negative Acute Lymphoblastic Leukemia: A Phase 2 Clinical Trial. JAMA Oncol. 2018;4(2):230-234. doi:10.1001/jamaoncol.2017.2380.

7e. Kantarjian H, Ravandi F, Short NJ, Huang X, Jain N, Sasaki K, Daver N, Pemmaraju N, Khoury JD, Jorgensen J, et al. Inotuzumab ozogamicin in combination with low-intensity chemotherapy for older patients with Philadelphia chromosome-negative acute lymphoblastic leukaemia: a

single-arm, phase 2 study. Lancet Oncol. 2018 Feb;19(2):240-248. doi: 10.1016/S1470-2045(18)30011-1. Epub 2018 Jan 16. PMID: 29352703.

8e. Jain N, Maiti A, Ravandi F, et al. Inotuzumab ozogamicin with bosutinib for relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia or lymphoid blast phase of chronic myeloid leukemia. Am J Hematol. 2021 Aug 1;96(8):1000-1007. doi: 10.1002/ajh.26238. Epub 2021 May 28.

9e. Jabbour E, Sasaki K, Short NJ, et al. Long-term follow-up of salvage therapy using a combination of inotuzumab ozogamicin and mini-hyper-CVD with or without blinatumomab in relapsed/refractory Philadelphia chromosome-negative acute lymphoblastic leukemia. Cancer. 2021;127:2025-2038

10e. Prime Therapeutics Management. Besponsa Clinical Literature Review Analysis. Last updated April 2024. Accessed April 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 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 sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse

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 (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**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