

Besponsa™ (inotuzumab ozogamicin) (Intravenous)

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Dates Reviewed: 09/2017, 11/2018, 11/2019, 11/2020

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: 7 vials per 21 days

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

Cycle 1

- 27 billable units (2.7 mg) on Day 1, 18 billable units on Days 8 and 15 of a 21 to 28-day cycle

Subsequent Cycles (maximum of 5 cycles)

- 27 billable units (2.7 mg) on Day 1, 18 billable units on Days 8 and 15 of a 28-day cycle for up to 2 cycles
- 18 billable units (1.8 mg) on Day 1, Day 8, and Day 15 of a 28-day cycle for up to 3 cycles

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Baseline electrocardiogram (ECG) is within normal limits; **AND**
- Patient has not previously received inotuzumab ozogamicin; **AND**
- Patient has CD22-positive disease; **AND**

B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) † ¹⁻³

- Patient is at least 18 years of age; **AND**
 - Patient has relapsed or refractory disease; **AND**
 - Used as single agent therapy or in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine); **AND**

- Patient is Philadelphia chromosome (Ph)-negative; **OR**
- Patient is Philadelphia chromosome (Ph)-positive and failed previous therapy (i.e., intolerant or refractory) with a tyrosine kinase inhibitor (e.g., imatinib, dasatinib, ponatinib, nilotinib, bosutinib, etc.); **OR**
- Used as induction therapy in patients ≥ 65 years of age or with substantial comorbidities; **AND**
 - Used in combination with mini-hyper CVD; **AND**
 - Patient is Philadelphia chromosome (Ph)-negative

B-Cell Pediatric Acute Lymphoblastic Leukemia (ALL) †^{3,4}

- Patient is at least 2 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 failed previous therapy (i.e., intolerant or refractory) with a tyrosine kinase inhibitor (e.g., imatinib, dasatinib, etc.)

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s)

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration

Indication	Dose
B-Cell Precursor ALL	<p>Cycle 1:</p> <ul style="list-style-type: none"> • 1.8 mg/m² total per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²) • 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 <p>Subsequent Cycles (cycles are 4 weeks in duration):</p> <p><u>CR or CRi achieved</u></p> <ul style="list-style-type: none"> • 1.5 mg/m² total per cycle, administered as 3 divided doses on Day 1 (0.5 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²) <p><u>Did not achieve CR or CRi</u></p> <ul style="list-style-type: none"> • 1.8 mg/m² total per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²) • Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment. <p>Patients proceeding to HSCT:</p> <ul style="list-style-type: none"> • Recommended duration of treatment is 2 cycles

<ul style="list-style-type: none"> A third cycle may be considered for those patients who do not achieve CR or CRi and MRD negativity after 2 cycles <p>Patients not proceeding to HSCT:</p> <ul style="list-style-type: none"> Additional cycles of treatment, up to a maximum of 6 cycles, may be administered
<i>CR (complete remission); CRi (complete remission with incomplete hematologic recovery); HSCT (hematopoietic stem cell transplant); MRD (minimal residual disease)</i>

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

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

VII. References

- Besponsa [package insert]. Philadelphia, PA; Pfizer Inc., March 2018. Accessed September 2020.
- 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.
- Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) inotuzumab ozogamicin. National Comprehensive Cancer Network, 2020. 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 September 2020.
- 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. doi:10.1038/s41375-018-0265-z.
- Palmetto GBA, LLC. Local Coverage Article: Billing and Coding: Chemotherapy (A56141). Centers for Medicare & Medicaid Services, Inc. Updated on 05/26/2020 with effective date 04/30/2020. Accessed October 2020.

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)

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), Local Coverage Articles (LCAs), 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/LCA/LCD):

Jurisdiction(s): J & M	NCD/LCA/LCD Document (s): A56141
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAAA	

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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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