Clinical Policy: Inotuzumab Ozogamicin (Besponsa)

Reference Number: CP.PHAR.359
Effective Date: 09.26.17
Last Review Date: 11.17 Revision Log
Line of Business: Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Inotuzumab ozogamicin (Besponsa™) is a CD22-directed antibody-drug conjugate.

FDA Approved Indication(s)
Besponsa is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Besponsa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. B-Cell Precursor Acute Lymphoblastic Leukemia (must meet all)**:**

1. Diagnosis of relapsed or refractory B-cell ALL;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an oncologist;
4. B-cell ALL is CD22 positive;
5. B-cell ALL Philadelphia chromosome status meets (a or b):
   a. Philadelphia chromosome-negative;
   b. Philadelphia chromosome-positive and intolerant or refractory to tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, nilotinib, bosutinib, ponatinib);
6. Besponsa is prescribed as single-agent therapy;
7. Dose does not exceed 1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose).

Approval duration: Up to 6 cycles total

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. B-Cell Precursor Acute Lymphoblastic Leukemia (must meet all)**:**

1. Currently receiving medication via Centene benefit, or member has previously met initial approval criteria;
2. Member has not received ≥ 6 cycles of Besponsa;

3. If request is for a dose increase, new dose does not exceed 1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose).

Approval duration: Up to 6 cycles total

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CR: complete remission
CRi: complete remission with incomplete hematologic recovery
HSCT: hematopoietic stem cell transplant

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
B-cell ALL	*Pre-medication is recommended before each dose.* If proceeding to hematopoietic stem cell transplant (HSCT): • The recommended duration of treatment with Besponsa is 2 cycles. A third cycle may be considered for those patients who do not achieve a complete remission* (CR) or complete remission with incomplete hematologic recovery* (CRi) and minimal residual disease negativity after 2 cycles. If not proceeding to HSCT: • Additional cycles of treatment, up to a maximum of 6 cycles, may be administered. ***Cycle details:*** • For the first cycle: o The recommended total dose of Besponsa for all patients is 1.8 mg/m^2 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. • For subsequent cycles:	1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose)

Indication	Dosing Regimen	Maximum Dose
	○ In patients who achieve a CR or CRi, the recommended total dose of Besponsa is 1.5 mg/m^2 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). Subsequent cycles are 4 weeks in duration. OR ○ In patients who do not achieve a CR or CRi, the recommended total dose of Besponsa is 1.8 mg/m^2 per cycle given 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). Subsequent cycles are 4 weeks in duration. ○ Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment.	

**CR (complete remission) 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 (complete remission with incomplete hematologic recovery) 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. Product Availability

Single-dose vial, powder for reconstitution: 0.9 mg

VII. References

1. Besponsa prescribing information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc. August 2017. Available at http://labeling.pfizer.com/ShowLabeling.aspx?id=9503. Accessed September 2017.
2. Acute lymphoblastic leukemia (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed September 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.26.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.