

**Clinical Policy: Inotuzumab Ozogamicin (Besponsa)**

Reference Number: CP.PHAR.359

Effective Date: 09.26.17

Last Review Date: 11.21

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Inotuzumab ozogamicin (Besponsa<sup>™</sup>) 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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> 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 B-cell ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. B-cell ALL is CD22 positive;
4. Disease meets one of the following (a or b):
  - a. Philadelphia chromosome-negative, and one of the following (i or ii):
    - i. Disease is relapsed or refractory;
    - ii. Besponsa is prescribed as induction therapy, and either age  $\geq 65$  years or member has substantial comorbidities;
  - b. Philadelphia chromosome-positive, and both of the following (i and ii):
    - i. Disease is relapsed or refractory;
    - ii. Member is intolerant or refractory to tyrosine kinase inhibitor therapy (e.g., imatinib, Sprycel<sup>®</sup>, Tasigna<sup>®</sup>, Bosulif<sup>®</sup>, Iclusig<sup>®</sup>);\*
5. If age  $\leq 18$  years, Besponsa is prescribed as single-agent therapy;
6. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 1.8 mg/m<sup>2</sup> per cycle (0.8 mg/m<sup>2</sup> on Day 1 and 0.5 mg/m<sup>2</sup> on Days 8 and 15);
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*\*Prior authorization is required for tyrosine kinase inhibitor therapy*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration: Up to 6 cycles total**

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1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Besponsa for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not received  $\geq 6$  cycles of Besponsa;
4. If request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed  $1.8 \text{ mg/m}^2$  per cycle ( $0.8 \text{ mg/m}^2$  on Day 1 and  $0.5 \text{ mg/m}^2$  on Days 8 and 15);
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN.

**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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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

FDA: Food and Drug Administration

HSCT: hematopoietic stem cell transplant

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*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib (Gleevec®)	600 mg PO QD	600 mg/day
Sprycel (dasatinib)	140 mg PO QD	180 mg/day
Tasigna (nilotinib)	400 mg PO BID	800 mg/day
Bosulif (bosutinib)	400 -500 mg PO QD	600 mg/day
Iclusig (ponatinib)	45 mg PO QD	45 mg/day

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): none reported
- Boxed warning(s): hepatotoxicity, including hepatic venoocclusive disease; increased risk of post-HSCT non-relapse mortality

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
B-cell ALL	<p>If proceeding to hematopoietic stem cell transplant (HSCT):</p> <ul style="list-style-type: none"> <li>• The recommended duration 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.</li> </ul> <p>If not proceeding to HSCT:</p> <ul style="list-style-type: none"> <li>• Additional cycles of treatment, up to a maximum of 6 cycles, may be administered.</li> </ul> <p><b>Cycle details:</b> <i>Pre-medication is recommended before each dose.</i></p> <ul style="list-style-type: none"> <li>• For the first cycle: 1.8 mg/m<sup>2</sup> per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m<sup>2</sup>), Day 8 (0.5 mg/m<sup>2</sup>), and Day 15 (0.5 mg/m<sup>2</sup>). 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.</li> <li>• For subsequent cycles: <ul style="list-style-type: none"> <li>○ In patients who achieve a CR or CRi, 1.5 mg/m<sup>2</sup> per cycle, administered as 3 divided doses on Day 1 (0.5 mg/m<sup>2</sup>), Day 8 (0.5 mg/m<sup>2</sup>), and Day 15 (0.5 mg/m<sup>2</sup>). Subsequent cycles are 4 weeks in duration. OR</li> <li>○ In patients who do not achieve a CR or CRi, 1.8 mg/m<sup>2</sup> per cycle given as 3 divided doses on Day 1 (0.8</li> </ul> </li> </ul>	1.8 mg/m <sup>2</sup> per cycle (0.8 mg/m <sup>2</sup> per dose)

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Indication	Dosing Regimen	Maximum Dose
	mg/m <sup>2</sup> ), Day 8 (0.5 mg/m <sup>2</sup> ), and Day 15 (0.5 mg/m <sup>2</sup> ). Subsequent cycles are 4 weeks in duration. <ul style="list-style-type: none"> <li>○ Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment.</li> </ul>	

\*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  $\geq 100 \times 10^9/L$  and absolute neutrophil counts [ANC]  $\geq 1 \times 10^9/L$ ) 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  $< 100 \times 10^9/L$  and/or ANC  $< 1 \times 10^9/L$ ) 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.; March 2018. Available at [www.besponsa.com](http://www.besponsa.com). Accessed July 26, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed June 28, 2021.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2021. Available at nccn.org. Accessed July 26, 2021.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 2.2021. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/ped\\_all.pdf](https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf). Accessed July 15, 2021.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9229	Injection, inotuzumab ozogamicin, 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.26.17	11.17
4Q 2018 annual review: no significant changes; HIM-Medical added; added hematologist prescriber option, added continuity of care language to Section II; references reviewed and updated.	07.12.18	11.18
4Q 2019 annual review: FDA/NCCN dosing limitation added; age removed to encompass pediatrics per NCCN; references reviewed and updated.	08.27.19	11.19

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: added Commercial LOB; modified HIM-Medical Benefit to HIM line of business; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: added additional pathway for use as induction therapy and revised requirement for use as single agent therapy to only apply to pediatric ALL per NCCN; clarified dosing per FDA label; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	06.28.21	11.21

**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

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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.

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**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.

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