Clinical Policy: Inotuzumab Ozogamicin (Besponsa)

Reference Number: CP.PHAR.359
Effective Date: 09.26.17
Last Review Date: 11.25
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™) is a CD22-directed antibody and cytotoxic drug conjugate.

FDA Approved Indication(s)

Besponsa is indicated for the treatment of relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients 1 year and older.

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® 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. Age ≥ 1 year;
4. B-cell ALL is CD22 positive;
5. One of the following (a or b):
   a. Disease is relapsed or refractory;
   b. If prescribed as frontline therapy, age ≥ 18 years;
6. Besponsa is prescribed for no more than 6 cycles total;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 1.8 mg/m^2 per cycle (0.8 mg/m^2 on Day 1 and 0.5 mg/m^2 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*).

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

Approval duration:
Commercial – 6 months or to the member's renewal date, whichever is longer (*up to 6 cycles total*)
HIM/Medicaid – 6 months (*up to 6 cycles total*)

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 ≥ 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 mg/m^2 per cycle (0.8 mg/m^2 on Day 1 and 0.5 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:
Commercial – 6 months or to the member's renewal date, whichever is longer (*up to 6 cycles total)*
HIM/Medicaid – 6 months (*up to 6 cycles total*)

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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

Appendix B: Therapeutic Alternatives

Not Applicable

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	If proceeding to hematopoietic stem cell transplant (HSCT): • 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. If not proceeding to HSCT: • Additional cycles of treatment, up to a maximum of 6 cycles, may be administered. ***Cycle details:*** *Pre-medication is recommended before each dose.* • For the first cycle: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),	1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose)

Indication	Dosing Regimen	Maximum Dose
	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: o In patients who achieve a CR or CRi, 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 o In patients who do not achieve a CR or CRi, 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. o 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.; March 2024. Available at: https://besponsa.pfizerpro.com. Accessed July 15, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 23, 2025.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed August 23, 2025.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed August 23, 2022.

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
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
4Q 2022 annual review: for Philadelphia chromosome-positive disease removal of requirement of intolerant or refractory to TKI per NCCN; added to initial criteria Besponsa is prescribed for no more than 6 cycles total; approval duration revised to 6 months (up to 6 cycles total); references reviewed and updated. Template changes applied to other diagnoses/indications.	08.02.22	11.22
4Q 2023 annual review: removed monotherapy requirement since Besponsa also indicated as combination therapy for age ≤ 18 years per NCCN Compendium; corrected "and" to "or" for scenarios of either relapsed/refractory disease or Philadelphia chromosome-negative disease; references reviewed and updated.	08.06.23	11.23
RT4: updated criteria to include pediatric expansion for 1 year and older; for disease that is not replased or refractory and Philadelphia chromosome-negative, updated age to ≥ 15 years to reflect "adolescent and young adult" population per NCCN compendium.	05.13.24	
4Q 2024 annual review: removed criterion that Besponsa is prescribed as induction therapy for Philadelphia chromosome-negative disease per NCCN; revised Commercial approval durations to "6 months or to the member's renewal date, whichever is longer;" references reviewed and updated.	07.11.24	11.24
4Q 2025 annual review: removed criteria option for age ≥ 15 years for Philadelphia chromosome-negative per NCCN Compendium; added criteria option to relapsed or refractory disease when prescribed as frontline therapy and age ≥ 18 years per NCCN Compendium; references reviewed and updated.	07.15.25	11.25

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.