Clinical Policy: Inotuzumab Ozogamicin (Besponsa)

Reference Number: PA.CP.PHAR.359
Effective Date: 09/2017
Last Review Date: 10/2025

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 (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness 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, b or c):
   a. Disease is relapsed or refractory;
   b. If prescribed as frontline therapy, age ≥ 18 years;
   c. Other NCCN recommendations listed as category 1, 2A, or 2B;
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*).

Approval duration: 6 months Up to 6 cycles total

B. Other diagnoses/indications

1. Refer to PA.CP.PHAR.53 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 PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;

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*).

Approval duration: Up to 6 cycles total

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies; **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to PA.CP.PHAR.53 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 – PA.CP.PHAR.53 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:	1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose)

Indication	Dosing Regimen	Maximum Dose
	• 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), 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: ○ 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 ○ 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. ○ 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 www.besponsa.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 nccn.org. 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, 2025.

Reviews, Revisions, and Approvals	Date
New Policy Created	07/2018

Reviews, Revisions, and Approvals	Date
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: FDA/NCCN dosing limitation added; age removed to encompass pediatrics per NCCN; references reviewed and updated.	08/2020
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 reviewed and updated.	10/2021
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.	10/2022
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.	10/2023
4Q 2024 annual review: 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; references reviewed and updated.	10/2024
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.	10/2025