

## Clinical Policy: Inotuzumab Ozogamicin (Besponsa)

Reference Number: ERX.SPA.256

Effective Date: 12.01.18

Last Review Date: 11.21

Line of Business: Commercial, Medicaid

[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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions<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*).

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

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

##### B. Other diagnoses/indications

1. Refer to ERX.PA.01 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 a health plan affiliated with Envolve Pharmacy Solutions, 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 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. 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to ERX.PA.01 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 – ERX.PA.01 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*

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib (Gleevec <sup>®</sup> )	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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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 veno-occlusive 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):	1.8 mg/m <sup>2</sup> per cycle (0.8 mg/m <sup>2</sup> per dose)

Indication	Dosing Regimen	Maximum Dose
	<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: Pre-medication is recommended before each dose.</b></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 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.</li> </ul> </li> </ul> <p>Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment.</p>	

\*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

- Besponsa Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; March 2018. Available at [www.besponsa.com](http://www.besponsa.com). Accessed July 26, 2021.
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- National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2021. Available at nccn.org. Accessed July 26, 2021.
- 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.07.18	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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; 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 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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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