Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2021**
Policy Number: PA.CP.PHAR.359	**Effective Date: 01/2020** **Revision Date: 10/2021**
Policy Name: Inotuzumab Ozogamicin (Besponsa)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Inotuzumab Ozogamicin (Besponsa)

Reference Number: PA.CP.PHAR.359
Effective Date: 09.26.17
Last Review Date: 10/2021 Revision Log

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 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. 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 ≥ 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®, Tasigna®, Bosulif®, Iclusig®);*
      * *Prior authorization is required for tyrosine kinase inhibitor therapy*
5. If age ≤ 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^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: 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.LTSS.PHAR.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*).

**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 PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.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

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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	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), 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.	1.8 mg/m^2 per cycle (0.8 mg/m^2 per dose)

**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 2018. Available at 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. 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. Accessed July 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New Policy Created	07/31/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
4Q 2020 annual review: FDA/NCCN dosing limitation added; age removed to encompass pediatrics per NCCN; references reviewed and updated.	08/20	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.	10/2021	