# Medical Policy:

## Besponsa® (inotuzumab ozogamicin) Intravenous

| POLICY NUMBER | LAST REVIEW | ORIGIN DATE |
|---|---|---|
| MG.MM.PH.47 | February 27, 2025 | |



## Definitions

Besponsa (inotuzumab ozogamicin) is a humanized CD22-directed monoclonal antibody-drug conjugate which is composed of the IgG4 kappa antibody inotuzumab (which is specific for human CD22), a calicheamicin component (a cytotoxic agent that causes double-stranded DNA breaks), and an acid-cleavable linker that covalently binds the calicheamicin to inotuzumab. After the antibody-drug conjugate binds to CD22, the CD22-conjugate complex is internalized, and releases calicheamicin. Calicheamicin binds to the minor groove of DNA to induce double strand cleavage and subsequent cell cycle arrest and apoptosis.

Besponsa (inotuzumab ozogamicin) is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

## Length of Authorization

Coverage will be provided for 6 months (for up to a maximum of 6 cycles) and may not be renewed.

## Dosing Limits [Medical Benefit]

Max Units (per dose and over time): 63 billable units every 21 days (for up to a maximum of 6 cycles)

## Guideline

Besponsa (inotuzumab ozogamicin) may be considered medically necessary for the following diagnoses when subsequent criteria are met:

**I. INITIAL CRITERIA**

1. **Adult B-cell precursor acute lymphoblastic leukemia (ALL):**
   - A. Patient is 18 years of age or older; **AND**
   - B. Patient has CD22-positive disease; **AND**
   - C. Patient has relapsed or refractory disease; **AND**
   - D. Used as single agent therapy; **OR**
   - E. Used in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine); with or without blinatumomab as part of consolidation; **AND**
     - i. Patient is Philadelphia chromosome (Ph)-negative; **OR**
     - ii. Patient is Philadelphia chromosome (Ph)-positive and refractory to prior tyrosine kinase inhibitor therapy *(e.g., imatinib, dasatinib, ponatinib,nilotinib, bosutinib, etc.);* **OR**
   - F. Used in combination with tyrosine kinase inhibitor (TKI) therapy *(e.g., bosutinib, dasatinib, imatinib, nilotinib, or ponatinib)*; **AND**
     - i. Patient is Philadelphia chromosome (Ph)-positive; **OR**
   - G. Used as frontline consolidation therapy **AND** *(Note: May be used with rituximab for AYA or adults <65 years of age without substantial comorbidities)*
   - H. Used as combination with mini-hyper-CVD, with or without blinatumomab; **AND**
     - i. Patient is Philadelphia chromosome (Ph)-positive; **OR**
   - I. Patient has persistent/rising minimal/measurable residual disease (MRD); **AND**
     - i. Used as single agent therapy; **OR**
     - ii. Used in combination with TKI therapy; **AND**
       - a. Patient is Philadelphia chromosome (Ph)-positive

2. **Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia (ALL)**
   - A. Patient is at least 1 year of age; **AND**
   - B. Patient has relapsed or refractory disease**; AND**
     - i. Used as single agent therapy; **OR**
     - ii. Used in combination with mini-hyper-CVD (cyclophosphamide, vincristine, dexamethasone, methotrexate, cytarabine); **AND**.*)*
       - a. Patient has BCR::ABL1 negative disease

### Limitations/Exclusions

1. Approval will be granted for 6 months, and **may not be renewed**
2. Patient has not previously received treatment with inotuzumab ozogamicin; **AND**
3. Patient has CD22-positive disease; **AND**
4. Baseline electrocardiogram (ECG) is within normal limits prior to initiating therapy and will be periodically monitored during treatment.

## Applicable Procedure Codes

| Code | Description |
|---|---|
| J9229 | Injection, inotuzumab ozogamicin, 0.1 mg |

## Applicable NDCs

| Code | Description |
|---|---|
| 00008-0100-01 | Besponsa 0.9mg Solution Reconstituted J9229 Injection, inotuzumab ozogamicin, 0.1 mg |

## ICD-10 Diagnoses

| Code | Description |
|---|---|
| C83.50 | Lymphoblastic (diffuse) lymphoma, unspecified site |
| C83.51 | Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck |
| C83.52 | Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes |
| C83.53 | Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes |
| C83.54 | Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb |
| C83.55 | Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb |
| C83.56 | Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes |
| C83.57 | Lymphoblastic (diffuse) lymphoma, spleen |
| C83.58 | Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites |
| C83.59 | Lymphoblastic (diffuse) lymphoma, extranodal and solid organ site |
| C91.00 | Acute lymphoblastic leukemia not having achieved remission |
| C91.01 | Acute lymphoblastic leukemia, in remission |
| C91.02 | Acute lymphoblastic leukemia, in relapse |

## Revision History

| Company(ies) | DATE | REVISION |
|---|---|---|
| EmblemHealth & ConnectiCare | 2/27/2025 | Annual Review:<br>Removed: Max Units (per dose and over time):<br>Cycle 1: 27 billable units on Day 1, 18 billable units on Day 8 and Day 15 of a 21 to 28-day cycle<br>Subsequent Cycles (maximum of 5 cycles)<br>• 27 billable units on Day 1, 18 billable units on Day 8 and Day 15 of a 28-day cycle for up to 2 cycles<br>• 18 billable units on Day 1, Day 8, and Day 15 of a 28-day cycle for up to 3 cycles<br>Replaced with ): 63 billable units every 21 days (for up to a maximum of 6 cycles)<br><br>Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) – removed i. Patient is Philadelphia chromosome (Ph)-negative; OR<br>ii. Patient is Philadelphia chromosome (Ph)-positive; AND<br>a. Patient is intolerant or refractory to prior tyrosine kinase inhibitor (TKI) therapy (e.g. imatinib, dasatinib etc.) Replaced with ii. Used in combination with mini-hyper-CVD (cyclophosphamide, vincristine, dexamethasone, methotrexate, cytarabine); AND.) a. Patient has BCR::ABL1 negative disease<br><br>Adult B-cell precursor acute lymphoblastic leukemia (ALL): Removed - Used as induction therapy in patients ≥65 years of age or with substantial comorbidities; AND i. Used in combination with mini-hyper CVD; AND<br>ii. Patient is Philadelphia chromosome (Ph)-negative. Replaced with Used as frontline consolidation therapy AND (Note: May be used with rituximab for AYA or adults <65 years of age without substantial comorbidities) Used as |

<table>
<tr><td></td><td></td><td>combination with mini-hyper-CVD, with or without blinatumomab; AND Patient is Philadelphia chromosome (Ph)-positive; OR Patient has persistent/rising minimal/measurable residual disease (MRD); AND i. Used as single agent therapy; OR ii. Used in combination with TKI therapy; AND a. Patient is Philadelphia chromosome (Ph)-positive.<br><br>Addition to limitations/exclusions: Patient has not previously received treatment with inotuzumab ozogamicin; AND Patient has CD22-positive disease; AND Baseline electrocardiogram (ECG) is within normal limits prior to initiating therapy and will be periodically monitored during treatment.</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>4/1/2024</td><td>Annual Review: Added Pediatric ALL indication and criteria</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>7/25/2023</td><td>Annual Review:<br><u>B-cell precursor acute lymphoblastic leukemia (ALL):</u> Initial Criteria:<br>Removed wording “Besponsa will be used as single agent therapy; AND<br>iii. Patient is Philadelphia chromosome (Ph)-negative; OR<br>iv. Patient is Philadelphia chromosome (Ph)-positive and failed previous therapy with a tyrosine kinase inhibitor; AND<br>J. Besponsa will be used as single agent therapy.”<br>Added ” Used as single agent therapy; OR<br>K. Used in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine); AND<br>i. Patient is Philadelphia chromosome (Ph)-negative; OR<br>ii. Patient is Philadelphia chromosome (Ph)-positive and refractory to prior tyrosine kinase inhibitor therapy (e.g., imatinib, dasatinib, ponatinib,nilotinib, bosutinib, etc.); OR<br>L. Used in combination with tyrosine kinase inhibitor (TKI) therapy (e.g., bosutinib, dasatinib, imatinib, nilotinib, or ponatinib); AND<br>i. Patient is Philadelphia chromosome (Ph)-positive; OR<br>M. Used as induction therapy in patients ≥65 years of age or with substantial comorbidities; AND<br>i. Used in combination with mini-hyper CVD; AND<br>ii. Patient is Philadelphia chromosome (Ph)-negative”<br>Added ICD-10 Codes:
<table>
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| EmblemHealth & ConnectiCare | 4/04/2022 | Transferred policy to new template |
| EmblemHealth & ConnectiCare | 12/30/2020 | Annual review: no policy changes |
| EmblemHealth & ConnectiCare | 10/30/2019 | Annual review |
| EmblemHealth & ConnectiCare | 12/3/2018 | Added J9229 and removed C9028 from Applicable Procedure Codes. |

## References


1. Besponsa [package insert]. Philadelphia, PA; Pfizer Inc., March 2018. Accessed October 2019.
2. Kantarjian HM, DeAngelo DJ, Stelljes M, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. N Engl J Med. 2016 Aug 25;375(8):740-53.
3. 3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) inotuzumab ozogamicin. National Comprehensive Cancer Network, 2017. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2017.