SCOPE:
Superior HealthPlan Pharmacy Department, Medical Directors

PURPOSE:
It is the policy of Superior HealthPlan to follow state guidance for medical necessity review of inotuzumab ozogamicin (Besponsa®). This medication is a pass through drug and should follow state guidance for medical necessity review for Medicaid/CHIP due to the manner in which it is reimbursed. All determinations will be performed by a Superior Medical Director. A pharmacy clinician will review the prior authorization request and make a recommendation to the Medical Director but will not make the ultimate determination on any case.

BACKGROUND:
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).

Formulations:
Single-dose vial, powder for reconstitution: 0.9 mg

PROCEDURE:
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

I. Initial Approval Criteria:

1. A Medical Director is required to review and approve or deny all requests.
2. Diagnosis of precursor B-cell acute lymphoblastic leukemia (ALL) that is refractory or in relapse. (See section IV for definition of refractory or relapsed disease).
3. Age ≥ 18 years;
4. Prescribed by or in consultation with an oncologist;
5. The prescriber agrees to monitor the person for signs and symptoms of hepatic veno-occlusive disease during treatment of Besponsa®. Besponsa® is not a benefit for Members who have hepatic veno-occlusive disease.
6. Besponsa® is prescribed as single-agent therapy;
7. Dose does not exceed 1.8 mg/m² per cycle (0.8 mg/m² per dose).

Approval duration: Up to 6 cycles total

II. Continued Therapy
1. Currently receiving medication via Centene benefit, or member has previously met initial approval criteria or was on the therapy by another managed care organization;
2. A Medical Director is required to review and approve or deny all requests for continued treatment.
8. Diagnosis of precursor B-cell acute lymphoblastic leukemia (ALL) that is refractory or in relapse. (See section IV for definition of refractory or relapsed disease)
3. Age ≥ 18 years;
4. Prescribed by or in consultation with an oncologist originally;
9. The prescriber agrees to monitor the person for signs and symptoms of hepatic veno-occlusive disease during continued treatment of Besponsa®. Besponsa® is not a benefit for Members who have hepatic veno-occlusive disease.
5. Member has not received ≥ 6 cycles of Besponsa®;
6. If request is for a dose increase, new dose does not exceed 1.8 mg/m² per cycle (0.8 mg/m² per dose).

Approval duration: Up to 6 cycles total
III. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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</thead>
<tbody>
<tr>
<td>B-cell ALL</td>
<td>Pre-medication is recommended before each dose. If proceeding to hematopoietic stem cell transplant (HSCT): &lt;ul&gt;&lt;li&gt;The recommended duration of treatment with Besponsa® 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.&lt;/li&gt;&lt;li&gt;If not proceeding to HSCT:&lt;ul&gt;&lt;li&gt;Additional cycles of treatment, up to a maximum of 6 cycles, may be administered. <strong>Cycle details:</strong>&lt;ul&gt;&lt;li&gt;For the first cycle:&lt;ul&gt;&lt;li&gt;The recommended total dose of Besponsa® for all patients is 1.8 mg/m² per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²). 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.&lt;/li&gt;&lt;/ul&gt;• For subsequent cycles:&lt;ul&gt;&lt;li&gt;In patients who achieve a CR or CRi, the recommended total dose of Besponsa® is 1.5 mg/m² per cycle, administered as 3 divided doses on Day 1 (0.5 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²). Subsequent cycles are 4 weeks in duration. OR&lt;/li&gt;&lt;li&gt;In patients who do not achieve a CR or CRi, the recommended total dose of Besponsa® is 1.8 mg/m² per cycle.&lt;/li&gt;&lt;/ul&gt;&lt;/li&gt;&lt;/ul&gt;&lt;/li&gt;&lt;/ul&gt;&lt;/li&gt;&lt;/ul&gt;</td>
<td>1.8 mg/m² per cycle (0.8 mg/m² per dose)</td>
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**Policy and Procedure**

**DEPARTMENT:** Pharmacy, Medical Directors  
**DOCUMENT NAME:** inotuzumab ozogamicin (Besponsa®)

**PAGE:** 4 of 5  
**REPLACES DOCUMENT:**

**APPROVED DATE:** 4/6/18  
**RETIRED:**

**EFFECTIVE DATE:** 4/6/18  
**REVIEWED/REVISED:** 2/12/19, 2/04/20

**PRODUCT TYPE:** Star, Star Health, Star Kids, Star Plus, Chip, Chip Prenate  
**REFERENCE NUMBER:** TX.PHAR.47

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<td></td>
<td>1.8 mg/m² per cycle given as 3 divided doses on Day 1 (0.8 mg/m²), Day 8 (0.5 mg/m²), and Day 15 (0.5 mg/m²). Subsequent cycles are 4 weeks in duration. o Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment.</td>
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*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 × 10⁹/L and absolute neutrophil counts [ANC] ≥ 1 × 10⁹/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 × 10⁹/L and/or ANC < 1 × 10⁹/L) and resolution of any extramedullary disease.

**IV. Definition of relapse or refractory precursor B-cell acute lymphoblastic leukemia (ALL):**

Superior considers inotuzumab ozogamicin (Besponsa®) medically necessary for the treatment of adults (18 years of age or older) with relapsed or refractory CD22 positive (i.e., ≥5% blasts CD22-positive) B-cell precursor acute lymphoblastic leukemia (B-ALL) when either of the following criteria are met:

A. Member has Philadelphia chromosome-positive (Ph+) disease and has failed treatment with at least one tyrosine kinase inhibitor (e.g., imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), bosutinib (Bosulif), ponatinib (Iclusig)) and standard chemotherapy; or

B. Member has Ph- disease and has failed treatment with at least one induction chemotherapy regimen for ALL.

**REFERENCES:**
ATTACHMENTS:

DEFINITIONS/Abbreviations:

ALL: acute lymphoblastic leukemia
CR: complete remission
CRi: complete remission with incomplete hematologic recovery
HSCT: hematopoietic stem cell transplant

REVISION LOG

<table>
<thead>
<tr>
<th>REVISION</th>
<th>DATE</th>
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<tbody>
<tr>
<td>Changed “Justin M. Weiss, Sr. V.P., Pharmacy Operations” to “Karen</td>
<td>2/12/19</td>
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<tr>
<td>Tadlock, V.P., Pharmacy Operations ” Formatting</td>
<td></td>
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<tr>
<td>Added exclusion criteria per the Texas Medicaid Provider Procedures</td>
<td>2/4/2020</td>
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<td>Manual</td>
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POLICY AND PROCEDURE APPROVAL

Karen Tadlock, V.P., Pharmacy Operations Approval on file
Dr. David Harmon, Sr. V.P., Chief Medical Officer Approval on file
Pharmacy & Therapeutics Committee: Approval on file

NOTE: The electronic approval retained in Compliance 360, Centene's P&P management software, is considered equivalent to a physical signature.