Policy and Procedure

DEPARTMENT: Pharmacy, Medical Directors	**DOCUMENT NAME:** inotuzumab ozogamicin (Besponsa®)
PAGE: 1 of 5	**REPLACES DOCUMENT:**
APPROVED DATE: 4/6/18	**RETIRED:**
EFFECTIVE DATE: 4/6/18	**REVIEWED/REVISED:** 2/12/19, 2/04/20, 2/16/21
PRODUCT TYPE: Star, Star Health, Star Kids, Star Plus, Chip, Chip Perinate	**REFERENCE NUMBER:** TX.PHAR.47

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 Member 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. Dose does not exceed 0.8 mg/m^2 IV on day 1 and 0.5 mg/m^2 IV on days 8 and 15.

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.
3. 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)
4. Age ≥ 18 years;
5. Prescribed by or in consultation with an oncologist *originally*;
6. The prescriber agrees to monitor the Member 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.
7. Member has not received ≥ 6 cycles of Besponsa®;
8. If request is for a dose increase, new dose does not exceed 0.8 mg/m^2 IV on day 1 and 0.5 mg/m^2 IV on days 8 and 15.

Approval duration: Up to 6 cycles total

III. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

B-cell ALL	*Pre-medication is recommended before each dose.*
	If proceeding to hematopoietic stem cell transplant (HSCT):
	• 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.
	If not proceeding to HSCT:
	• Additional cycles of treatment, up to a maximum of 6 cycles, may be administered.
	Cycle details:
	• For the first cycle:
	  ○ The recommended total dose of Besponsa® for all patients is 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, the recommended total dose of Besponsa® is 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
		0.8 mg/m^2 IV on day 1 and 0.5 mg/m^2 IV on days 8 and 15

Indication	Dosing Regimen	Maximum Dose
	○ In patients who do not achieve a CR or CRi, the recommended total dose of Besponsa® is 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.*

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 (Tasygna), 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.

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REFERENCES: N/A

ATTACHMENTS: N/A

DEFINITIONS/Abbreviations:

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

REVISION LOG

REVISION	DATE
Changed "Justin M. Weiss, Sr. V.P., Pharmacy Operations" to "Karen Tadlock, V.P., Pharmacy Operations " Formatting	2/12/19
Added exclusion criteria per the Texas Medicaid Provider Procedures Manual	2/4/20
Formatting changes, removed requirement to be single agent therapy to align with state criteria, clarified max dose. Updated spelling from CHIP Prenate to Perinate for Product Type.	2/16/21

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 RSA Archer, Centene's P&P management software, is considered equivalent to a physical signature.