Medical Drug Clinical Criteria

Subject:	Besponsa (inotuzumab ozogamicin)		
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Overview

This document addresses the use of Besponsa (inotuzumab ozogamicin). Besponsa is an antibody-drug conjugate composed of a monoclonal antibody targeting CD22 and the cytotoxic agent calicheamicin, which is released into the malignant cells upon binding. It is used to treat acute lymphoblastic leukemia (ALL), and should only be used in CD22+ B-cell ALL due to its molecular target.

The FDA approved Besponsa for CD22+ B-cell precursor ALL based on a phase 3 study (Kantarjian 2017). Besponsa monotherapy was compared to investigator's choice of standard therapy for patients age 18 years or older with relapsed or refractory, philadelphia chromosome (Ph)- positive or Ph-negative ALL. All patients had an Eastern Cooperative Oncology Group Performance Status (ECOG) of ≤2. Though only FDA approved for use in adults, the National Comprehensive Cancer Network® (NCCN) guidelines on Pediatric ALL recommend treatment with Besponsa for younger individuals as well. NCCN additionally recommends the use of Besponsa in combination with a tyrosine kinase inhibitor (bosutinib, dasatinib, imatinib, nilotinib, or ponatinib) or mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) with or without blinatumumab in the relapse/refractory setting. NCCN also recommends Besponsa as induction therapy for Philadelphia chromosome-negative disease in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine).

Besponsa has a black box warning for hepatotoxicity, including fatal and life-threatening hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS). Risk of VOD was greater in patient who underwent hematopoietic stem cell transplant (HSCT) after Besponsa treatment; other risk factors include liver disease, increased age, later salvage lines, and a greater number of Besponsa treatment cycles. Besponsa should be permanently discontinued if VOD occurs. Besponsa also has a black box warning for increased risk of post-HSCT non-relapse mortality because day 100 post-HSCT mortality was higher in patients receiving Besponsa.

Definitions and Measures

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Besponsa (inotuzumab ozogamicin)

Requests for Besponsa (inotuzumab ozogamicin) may be approved if the following criteria are met:

I. Individual has a diagnosis of CD22+ B-cell acute lymphocytic leukemia (ALL); **AND**
II. Individual meets all of the following:
    A. Relapsed or refractory disease; **AND**
    B. Individual is using Besponsa as (NCCN 1/2A):
        1. A single agent; **OR**
        2. In combination with a tyrosine kinase inhibitor (bosutinib, dasatinib, imatinib, nilotinib, or ponatinib); **OR**

3. In combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) with or without blinatumomab;

OR

III. Individual has a diagnosis of CD22+ B-cell acute lymphocytic leukemia (ALL) (NCCN 2A); **AND**
IV. Individual is using Besponsa as induction therapy for Philadelphia chromosome-negative disease; **AND**
V. Individual is using Besponsa in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine).

Requests for Besponsa (inotuzumab ozogamicin) may not be approved if the above criteria are not met and for all other indications not included above.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9229	Injection, inotuzumab ozogamicin, 0.1 mg [Besponsa]

ICD-10 Diagnosis

C91.00-C91.02	Acute lymphoblastic leukemia (ALL)
D46.A	Refractory cytopenia with multilineage dysplasia

Document History

Revised: 02/24/2023
Document History:

- 02/24/2023 – Annual Review: Update criteria to include combination use with a TKI or mini-hyper CVD per NCCN; include use as induction therapy per NCCN; remove ECOG performance status requirement; remove specific may not approve language. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: No changes. Coding Review: No changes.
- 02/21/2020 – Annual Review: Remove age from criteria. Coding Reviewed: Added ICD-10-CM D46.A
- 05/17/2019 – Annual Review: First review of Besponsa clinical criteria. Add reference for off label criteria. Coding reviewed: No changes.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 20, 2023.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Kantarjian HM, DeAngelo DJ, Stelljes M, et al. Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia. N Engl J Med. 2016; 375(8):740-753.
4. Kantarjian H, Ravandi F, Short NJ, et al. Inotuzumab ozogamicin in combination with low-intensity chemotherapy for older patients with Philadelphia chromosome-negative acute lymphoblastic leukaemia: a single-arm, phase 2 study. Lancet Oncol 2018;19:240-248.
5. Jabbour E, Ravindi F, Kebriaei P, et al. Salvage chemoinnunotherapy with inotuzumab ozogamicin combined with mini-Hyper-CVD for patients with relapsed or refractory Philadephia chromosome-negative acute lymphoblastic leukemia: A phase 2 clinical trial. JAMA oncol 2018; 4:230-234.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 20, 2023.
    a. Pediatric Acute lymphoblastic Leukemia. V1.2023. Revised November 9, 2022.
    b. Acute Lymphoblastic Leukemia. V1.2022. Revised April 4, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.