Clinical Criteria

Subject:	Besponsa (inotuzumab ozogamicin)		
Document #:	ING-CC-0131	**Publish Date:**	~~03/23/2021~~03/28/2022
Status:	~~Reviewed~~Revised	**Last Review Date:**	~~02/19/2021~~02/25/2022

Table of Contents

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. To date, Besponsa has not been thoroughly studied as first-line therapy for ALL or in combination with other chemotherapy agents. 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.

Other Uses

The safety and efficacy of Besponsa in combination with other agents is under investigation. The National Comprehensive Cancer Network® (NCCN) guidelines for ALL recommend Besponsa in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) in the relapse/refractory setting and as a moderate intensity induction therapy option for older adults or those with comorbidities. The combination use with hyper-CVD in the salvage setting was investigated in a single-arm phase 2 study (Jabbour 2018). A total of 59 individuals (ECOG 0-3) were treated with 8 cycles of hyper-CVD with inotuzumab on day 3 of the first 4 cycles. After a median follow up of 24 months, the median relapse-free survival and overall survival were 8 and 11 months, respectively. This combination regimen was also studied as induction therapy in 52 older adults (≥60 yo, ECOG 0-3) with Philadelphia chromosome-negative ALL in a phase 2 single-arm study (Kantarjian 2018). The progression free survival at 2 years was 59%. Adverse events in these trials included veno-occlusive disease (1 treatment-related death), thrombocytopenia, and infection. NCCN also recommends Besponsa in combination with bosutinib for relapsed/refractory Philadelphia chromosome-positive B-ALL, but supportive studies are not available to date.

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

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours

- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

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. Current Eastern Cooperative Oncology (ECOG) performance status of 0-2 (Kantarjian 2017).

Requests for Besponsa (inotuzumab ozogamicin) may not be approved for the following:

~~I. All other indications not included above; **OR**~~
~~II.~~I. Individual is using as first-line therapy for ALL; **OR**
II. Individual is using in combination with other chemotherapy agents; **OR**
III. When the above criteria are not met and for all other indications.

Formatted: Indent: Left: 0.5", No bullets or

Formatted: Font: Bold

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: 02/25/2022
Document History:

- 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. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 18, 2022.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. 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.
5. 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.
6. 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.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
8. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 18, 2022.
    a. Pediatric Acute lymphoblastic Leukemia. V1.2022. Revised October 1, 2021.
    b. Acute Lymphoblastic Leukemia. V4.2021. Revised January 7, 2022.