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Inotuzumab Ozogamicin

(Besponsa®) J9229 (0.1 mg)

Covered with prior authorization

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

- Individual has a diagnosis of CD22+ B-cell precursor acute lymphoblastic leukemia (ALL); **AND**
- Individual meets all of the following:
  - Relapsed or refractory disease; **AND**
  - Current Eastern Cooperative Oncology (ECOG) performance status of 0-2 (Kantarjian 2017).

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

Initial and renewal authorizations are for up to 12 months.

Annual reauthorizations will require medical chart documentation that the patient has been seen within the past 12 months and that markers of disease are improved by therapy.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Exclusion criteria:

- Besponsa® (inotuzumab ozogamicin) may not be approved when the above criteria are not met and for all other indications.
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use.
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk.
- Individual is using as first-line therapy for ALL.
- Individual is using in combination with other chemotherapy agents.

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U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage. 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 aged 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 patients 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®. Besponsa® also has a **black box warning** for hepatotoxicity including fatal and life-threatening VOD (also known as sinusoidal obstruction syndrome).

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Key References Accessed 8/2022:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. 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.
3. 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 leukemia: a single-arm, phase 2 study. Lancet Oncol 2018;19:240-248.
4. Jabbour E, Ravindi F, Kebriaei P, et al. Salvage chemoimmunotherapy with inotuzumab ozogamicin combined with mini-Hyper-CVD for patients with relapsed or refractory Philadelphia chromosome-negative acute lymphoblastic leukemia: A phase 2 clinical trial. JAMA oncol 2018; 4:230-234.
5. 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.
    a. Pediatric Acute lymphoblastic Leukemia. V1.2022. Revised October 1, 2021.
    b. Acute Lymphoblastic Leukemia. V4.2021. Revised January 7, 2022.

Date	Summary of Changes
August 2022	Criteria for use summary developed by the Ascension Medical Specialty Prior Authorization Team.
September 2022	Criteria for use summary approved by the Ascension Ambulatory Care Expert Review Panel.
October 2022	Criteria for use summary approved by the Ascension Therapeutic Affinity Group.

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team, or email your questions to smarthealthspecialty@ascension.org.