Inotuzumab Ozogamicin

NDC CODE(S) 00008-0100-XX BESPONSA 0.9MG Solution Reconstituted (PFIZER U.S.)

DESCRIPTION

Inotuzumab ozogamicin is a CD22-directed antibody-drug conjugate (ADC). It consists of three components: the IgG4 antibody inotuzumab which is specific for CD22, N-acetyl-gamma-calicheamicin which causes double stranded DNA breaks and an acid-cleavable covalent linker known as dimethylhydrazide.

Its anticancer activity is likely due to the binding of inotuzumab ozogamicin to CD22-expressing tumor cells followed by the internalization of the ADC-CD22 complex. Within the cell, the N-acetyl-gamma-calicheamicin is released and activated, inducing double-strand DNA breaks leading to cell cycle arrest and death by apoptosis.

POLICY

- Inotuzumab ozogamicin for the treatment of acute lymphoblastic leukemia (ALL) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Inotuzumab ozogamicin for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Inotuzumab ozogamicin is considered **medically appropriate** if **ALL** of the following:
  - Baseline Electrocardiogram (ECG) that is within normal limits
  - Individual has not previously received inotuzumab ozogamicin
  - Disease is CD22 positive
  - Diagnosis of **ANY ONE** of the following:
    - B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) if **ALL** of the following
      - Individual is 18 years of age or older
      - Disease is relapsed or refractory
      - Used as **ANY ONE** of the following:
        - Single agent therapy or in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) for disease that is **ANY ONE** of the following:
          - Philadelphia chromosome (Ph)-negative
          - Philadelphia chromosome-positive and failed previous therapy (i.e., intolerant or refractory) with a tyrosine kinase inhibitor (e.g., imatinib, dasatinib, ponatinib, nilotinib, bosutinib, etc.)
        - Induction therapy in individuals ≥65 years of age or with substantial comorbidities if **ALL** of the following:
          - Used in combination with mini-hyper CVD
          - Individual is Philadelphia chromosome (Ph)-negative
    - B-Cell Pediatric Acute Lymphoblastic Leukemia if **ALL** of the following:
      - Individual is 2 years of age or older
      - Disease is relapsed or refractory
      - Used as single agent therapy
      - Individual is **ANY ONE** of the following:
        - Philadelphia chromosome (Ph)-negative

- Philadelphia chromosome-positive and failed previous therapy (e.g., intolerant or refractory) with a tyrosine kinase inhibitor (e.g., imatinib, dasatinib, etc.)

RENEWAL CRITERIA

Inotuzumab ozogamicin is **NOT** considered **medically appropriate** for renewal

INDICATION(S)	DOSAGE & ADMINISTRATION
B-cell Precursor Acute Lymphoblastic Leukemia (ALL)	**Cycle 1:** 1.8 mg/m2 total 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
	Subsequent Cycles (cycles are 4 weeks in duration): **CR or CRi achieved** 1.5 mg/m2 total 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) **Did not achieve CR or CRi** 1.8 mg/m2 total 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) Those who do not achieve a CR or CRi within 3 cycles should discontinue treatment.
	If proceeding to HSCT, Recommended duration of treatment is 2 cycles A third cycle may be considered for those who do not achieve CR or CRi and MRD negativity after 2 cycles
	If not proceeding to HSCT, Additional cycles of treatment, up to a maximum of 6 cycles, may be administered
CR (complete remission); CRi (complete remission with incomplete hematologic recovery); HSCT (hematopoietic stem cell transplant); MRD (minimal residual disease) ~~Refrigerate (2-8°C; 36-46°F) and store in the original carton to protect from light. Do not freeze.~~	

LENGTH OF AUTHORIZATION

Coverage will be provided for 6 months (for up to a maximum of 6 cycles) and may not be renewed

Click here to view **DOSAGE LIMITS**

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with **Tennessee Code Annotated Section 56-7-2352** regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Bhojwani, D., Sposto, R., Shah, N. N., Rodriguez, V., Yuan, C., Stetler-Stevenson, M., et al. (2018). Inotuzumab ozogamicin in pediatric patients with relapsed/refractory acute lymphoblastic leukemia. *Leukemia,* 2019 (33), 884-892.

Lexicomp Online. (2020). AHFS DI. *Inotuzumab ozogamicin.* Retrieved November 18, 2020 from Lexicomp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, September). *Inotuzumab ozogamicin*. Retrieved November 18, 2020 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. *Inotuzumab ozogamicin.* Retrieved November 18, 2020 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2017, August). Center for Drug Evaluation and Research. *Besponsa® (inotuzumab ozogamicin) for injection, for intravenous use.* Retrieved November 18, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761040s000lbl.pdf.

EFFECTIVE DATE 4/2/21

ID_MRx