CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Inotuzumab Ozogamicin (Besponsa®)

Version: 1.0

EFFECTIVE DATE: 1/1/2025

NantHealth® | Eviti®

Please note the following:

Inotuzumab Ozogamicin (Besponsa®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Inotuzumab Ozogamicin (Besponsa): Discussion

Inotuzumab ozogamicin is a CD22-directed antibody drug conjugate (ADC). Inotuzumab ozogamicin recognizes human CD22. The small molecule, N-acetyl-gamma-calicheamicin, is a cytotoxic agent that is covalently attached to the antibody via a linker.[1]

It's an anti-CD22 monoclonal antibody-calicheamicin conjugate that binds to CD22-expressing tumor cells. Upon binding, the complex is internalized and the cytotoxic calicheamicin derivative is released inside the cell, inducing double-strand DNA breakage and subsequent cell death.[2]

Inotuzumab ozogamicin is approved by the Food and Drug Administration (FDA) for acute lymphoblastic leukemia (ALL).

Significant adverse reactions that can be associated with inotuzumab ozogamicin include myelosuppression, QT interval prolongation, and embryo-fetal toxicity. The most common adverse reactions (≥ 20% of patients) include laboratory abnormalities, thrombocytopenia, pyrexia, neutropenia, infection, anemia, vomiting, leukopenia, hemorrhage, fatigue, nausea, febrile neutropenia, headache, transaminases increase, abdominal pain, gamma-glutamyl transferase increase, and hyperbilirubinemia.[1]

The National Comprehensive Cancer Network (NCCN) endorses inotuzumab ozogamicin for acute lymphoblastic leukemia (ALL).[3]

Inotuzumab Ozogamicin: Definitions

- **AYA (Adolescents and Young Adults)** - Individuals within the range of 15 to 39 years of age.[4]
- **BCR-ABL1** - Break point cluster region (BCR) and Abelson (ABL) genes fuse together to form the BCR-ABL gene sequence.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **N-acetyl-gamma-calicheamicin** - A potent antitumor antibiotic derived from bacterium micromonospora echinospora. It is known for its ability to bind to DNA and induce double-strand breaks, leading to cell death.

Inotuzumab Ozogamicin: Policy

Note: Coverage of inotuzumab ozogamicin will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Inotuzumab ozogamicin will be considered for coverage when the following criteria are met:

Pediatric Acute Lymphoblastic Leukemia (ALL)

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Relapsed or refractory CD22-positive B-cell precursor ALL; OR

For **NCCN** required criteria coverage:

4. Single agent for one of the following:
   a) Relapsed/refractory break point cluster region (BCR)-Ableson (ABL)1-negative
   b) Relapsed/refractory BCR-ABL1-positive TKI intolerant/refractory; OR
5. Relapsed/refractory BCR-ABL1-negative B-ALL in combination with mini-hyper-CVD (mini-hyperfractionated cyclophosphamide, vincristine, dexamethasone, methotrexate, and cytarabine) regimen.

Acute Lymphoblastic Leukemia (ALL)

1. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

2. Relapsed or refractory CD22-positive B-cell precursor ALL; OR

For **NCCN** required criteria coverage:

3. Induction therapy for patients ≥65 years of age as a component of one of the following:
   a) ALL-INITIAL-1 (inotuzumab ozogamicin, dexamethasone)
   b) ALLIANCE A041703; OR

   Note: The above regimens are used for patients with substantial comorbidities with Philadelphia chromosome-negative B-ALL for one of the following:
   a) Frontline therapy
   b) Refractory therapy
   c) Late relapse (>3 years from initial diagnosis) if regimen was used in frontline

4. Therapy for patients at least 15 years of age as a component of inotuzumab ozogamicin + mini-hyperCVD in induction/consolidation (cyclophosphamide, vincristine, dexamethasone, inotuzumab ozogamicin alternating with cytarabine, methotrexate, inotuzumab ozogamicin with or without sequential blinatumomab as part of consolidation) for one of the following:
   a) Frontline therapy for adults with Philadelphia chromosome-negative B-ALL
   b) Relapsed/refractory therapy for Philadelphia chromosome-negative B-ALL
   c) Consideration for Philadelphia chromosome-positive B-ALL if refractory to TKIs; OR

   Note: There is data to support the benefit of rituximab for CD20-positive disease, in addition to chemotherapy (excluding immunotherapy), for adults under 65 years of age without substantial comorbidities (especially if under 60 years), if the minimal/measurable residual disease (MRD) is negative or unavailable for Philadelphia chromosome-negative B-ALL.

5. Therapy for patients at least 15 years of age for one of the following:
   a) Single agent if persistent/rising minimal/measurable residual disease (MRD) for B-ALL (AYA without substantial comorbidities and adults) during frontline consolidation therapy
   b) In combination with a TKI if persistent/rising MRD for Philadelphia chromosome-positive B-ALL (AYA without substantial comorbidities and adults) during frontline consolidation therapy
   c) Single agent for B-ALL (preferred for Philadelphia chromosome-negative) during relapsed/refractory (R/R) therapy
   d) In combination with a TKI for Philadelphia chromosome-positive B-ALL during R/R therapy

   Note: There is data to support the benefit of rituximab in addition to chemotherapy (excluding immunotherapy) for (AYA and adults <65 years of age) without substantial comorbidities with CD20-positive disease (especially in patients <60 years of age).
   For Philadelphia chromosome-positive B-ALL:
   1) TKI options include: bosutinib, dasatinib, imatinib, nilotinib, or ponatinib
   2) Imatinib use in first-line should be restricted to those who cannot tolerate broader acting TKIs

3) TKI/mutation contraindications: bosutinib - T315I, V299L, G250E, or F317L; dasatinib - T315I/A, F317L/V/I/C or V299L; imatinib - as per the NCCN guideline; nilotinib - T315I, Y253H, E255K/V, F359V/C/I or G250E.[4]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Inotuzumab Ozogamicin: References

1. Inotuzumab Ozogamicin (Besponsa) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761040s003lbl.pdf. Accessed December 4, 2024.
2. Wiedemeyer et al. ABBV-011, A Novel, Calicheamicin-Based Antibody–Drug Conjugate, Targets SEZ6 to Eradicate Small Cell Lung Cancer Tumors. https://pmc.ncbi.nlm.nih.gov/articles/PMC9381089/. Accessed December 4, 2024.
3. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed December 4, 2024.
4. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed December 4, 2024.

Inotuzumab Ozogamicin: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C91.0	Acute lymphoblastic leukemia
J9229	Inotuzumab ozogamicin

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Inotuzumab Ozogamicin: Revision and Review History

NO.	DESCRIPTION	DATE(S)
1	Original Effective Date:	1/1/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	1/24/2025
6	Revision Changes:	