CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Dinutuximab (Unituxin®)

Version: 1.0

EFFECTIVE DATE: 12/1/2024

NantHealth® | Eviti®

Please note the following:

Dinutuximab (Unituxin®)

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.

Dinutuximab (Unituxin): Discussion

Dinutuximab targets disialoganglioside (GD2) in neuroblastoma cells, attaches to these cells, and makes them a target for the body's immune system, thus eliminating cancer cells. It induces the lysis of cells expressing GD2 through complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), and direct cytotoxicity. In addition, dinutuximab may prevent interactions between the circulating malignant cells and the extracellular matrix.[1]

Dinutuximab is approved by the Food and Drug Administration (FDA) for neuroblastoma.

Dinutuximab may cause serious and potentially life-threatening infusion reactions, as well as severe neurologic adverse reactions, including neuropathic pain and peripheral neuropathy. It can lead to capillary leak syndrome, hypotension, bone marrow suppression, atypical hemolytic uremic syndrome, and embryo-fetal toxicity.[2]

The National Comprehensive Cancer Network (NCCN) endorses dinutuximab in the following cancer types: neuroblastoma.[3]

Dinutuximab: Definitions

- **Complement-Dependent Cytotoxicity (CDC)/Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)** - Immune-mediated cell destruction mechanisms which are triggered when Fc receptors are expressed on natural killer cells, macrophages, and other cells which are activated through binding with Fc receptors on monoclonal antibodies.[4]
- **GD2 Expression** - A glycosphingolipid that is stably expressed on the surface of tumor cells, making it a suitable candidate for targeting antibodies or chimeric antigen receptors. GD2 plays an important role in tumorigenesis. Its functions include proliferation, invasion, motility, and metastasis. Its high expression and ability to transform the tumor microenvironment may be associated with a malignant phenotype.[5]
- **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.

- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the 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.

Dinutuximab: Policy

Note: Coverage of dinutuximab 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.

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

Neuroblastoma

For **FDA** required criteria coverage:

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. In combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy[2]; OR

For **NCCN** required criteria coverage:

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Chemoimmunotherapy in combination with temozolomide, irinotecan, and sargramostim following induction for high-risk disease for one of the following:
   a) Minor response or stable disease (as bridging therapy to standard consolidation)
   b) Progressive disease; OR
4. Post-consolidation therapy in combination with sargramostim and isotretinoin following consolidation for high-risk disease and full disease evaluation with no disease progression; OR
5. Chemoimmunotherapy in combination with temozolomide, irinotecan, and sargramostim in patients with progressive disease following consolidation for high-risk disease.[3]

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

Dinutuximab: References

1. Mohd at el. Safety and efficacy of dinutuximab in the treatment of neuroblastoma: A review. https://pmc.ncbi.nlm.nih.gov/articles/PMC10729685/. Accessed November 19, 2024.
2. Dinutuximab Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125516s025lbl.pdf. Accessed November 19, 2024.
3. National Comprehensive Cancer Network. Neuroblastoma. https://www.nccn.org/professionals/physician_gls/pdf/neuroblastoma.pdf. Accessed November 19, 2024.
4. Malik at el. Understanding How Monoclonal Antibodies Work. https://www.ncbi.nlm.nih.gov/books/NBK572118/. Accessed November 19, 2024.
5. Philippova at el. GD2-targeting therapy: a comparative analysis of approaches and promising directions. https://pmc.ncbi.nlm.nih.gov/articles/PMC10979305/. Accessed November 19, 2024.

Dinutuximab: 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
C74.0	Malignant neoplasm of the adrenal gland
C74.9	Neuroblastoma
J1246	Dinutuximab

Dinutuximab: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	12/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	12/21/2024
6	Revision Changes:	