CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL ONCOLOGY

Daratumumab (Darzalex®)

Version: 1.0

EFFECTIVE DATE: 1/1/2024

NantHealth® | Eviti®

Please note the following:

Daratumumab (Darzalex®)

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.

Daratumumab (Darzalex): Discussion

Daratumumab is a CD38-targeted monoclonal antibody that attaches itself to the CD38 protein on the surface of hematopoietic cells, including multiple myeloma and other cell types and tissues. Daratumumab bound to CD38 inhibits the growth of CD38-expressing tumor cells by inducing cell death. [1,2]

Daratumumab is a CD38-directed cytolytic antibody approved by the FDA for the treatment of adult patients with multiple myeloma:

1. In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant, or in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
2. In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for an autologous stem cell transplant
3. In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for an autologous stem cell transplant
4. In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
5. In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
6. In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor
7. As monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double-refractory to a PI and an immunomodulatory agent. [2]

The National Comprehensive Cancer Network (NCCN) endorses daratumumab in the following cancer types: acute lymphoblastic leukemia, multiple myeloma, and systemic light chain amyloidosis. [3,4,5]

Daratumumab: Definitions

- **CD38 protein** – A glycoprotein that plays a role in cell adhesion, migration, and signal transduction. [6]
- **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.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of thirty-two 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.

Daratumumab: Policy

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

Acute Lymphoblastic Leukemia

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. As single-agent therapy for relapsed/refractory T-ALL [3]

Multiple Myeloma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Primary therapy for symptomatic multiple myeloma for transplant candidates in combination with one of the following:
    a) Bortezomib, lenalidomide, and dexamethasone
    b) Bortezomib, thalidomide and dexamethasone
    c) Carfilzomib, lenalidomide, and dexamethasone; OR
4. Primary therapy for symptomatic multiple myeloma for non-transplant candidates in combination with bortezomib, melphalan hydrochloride, and prednisone; OR
5. Primary therapy for symptomatic multiple myeloma or for disease relapse after 6 months following primary induction therapy with the same regimen in combination with one of the following:
    a) Lenalidomide and dexamethasone for non-transplant candidates
    b) Cyclophosphamide, bortezomib, and dexamethasone of regardless of transplant status; OR
6. Maintenance therapy for symptomatic multiple myeloma as a single agent for transplant candidates for one of the following:
    a) After the response to primary myeloma therapy

b) For response or stable disease following an autologous hematopoietic cell transplant (HCT)
c) For response or stable disease following a tandem autologous or allogeneic HCT for high-risk patients; OR

7. Therapy for previously treated multiple myeloma for relapse or for progressive disease for one of the following:
   a) In combination with bortezomib and dexamethasone if lenalidomide refractory
   b) In combination with carfilzomib and dexamethasone
   c) In combination with lenalidomide and dexamethasone if bortezomib refractory
   d) In combination with pomalidomide and dexamethasone in patients who have received one prior therapy, including lenalidomide and a proteasome inhibitor
   e) In combination with cyclophosphamide, bortezomib, and dexamethasone
   f) As a single agent in patients who have received at least three prior therapies, including a proteasome inhibitor and an immunomodulatory agent, or who are double refractory to a proteasome inhibitor and an immunomodulatory agent
   g) In combination with selinexor and dexamethasone[4]

Systemic Light Chain Amyloidosis

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. As a single agent for the treatment for relapsed/refractory disease [5]

Note: Coverage of daratumumab 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.

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

Daratumumab: References

1. Darzalex Multiple Myeloma Resources. https://www.darzalexhcp.com/multiple-myeloma-resources. Accessed June 6, 2023.
2. Daratumumab (Darzalex) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761036s044lbl.pdf. Accessed June 7, 2023.
3. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed June 7, 2023.
4. National Comprehensive Cancer Network Guidelines. Multiple Myeloma (Version 3.2023). https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed June 6, 2023.

5. National Comprehensive Cancer Network Guidelines. Systemic Light Chain Amyloidosis (Version 2.2023). https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed June 6, 2023.
6. Unraveling the mysteries of plasma cells. https://www.sciencedirect.com/topics/neuroscience/cd38. Accessed June 6, 2023.

Daratumumab: 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
C90.0	Multiple Myeloma
C91.00-C91.02	Acute lymphoblastic leukemia
E85.81	Systemic Light Chain Amyloidosis
J9145	Daratumumab (Darzalex®)

Daratumumab: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	6/28/2023
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	9/6/2023
6	Revision Changes:	