CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Ixazomib Citrate (Ninlaro®)

Version: 1.0

EFFECTIVE DATE: 1/1/2025

NantHealth® | Eviti®

Please note the following:

Ixazomib Citrate (Ninlaro®)

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.

Ixazomib Citrate (Ninlaro): Discussion

Ixazomib citrate is a second-generation proteasome inhibitor. It is hydrolyzed to its active form, MLN2238, which inhibits the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome, leading to apoptosis in multiple myeloma cells.[1,2]

Ixazomib citrate is rapidly absorbed and has a high volume of distribution, allowing better drug distribution from blood to tissue compartments which shows improved tumor-proteasome inhibition compared to bortezomib, leading to significant antitumor activity.

Ixazomib citrate is approved by the Food and Drug Administration (FDA) for multiple myeloma.

The most common adverse reactions associated with ixazomib citrate is thrombocytopenia, gastrointestinal toxicities, peripheral neuropathy, peripheral edema, cutaneous reactions, thrombotic microangiopathy, hepatotoxicity, and embryo-fetal toxicities.[2]

The National Comprehensive Cancer Network (NCCN) endorses ixazomib citrate for the following cancer types: multiple myeloma, systemic light chain amyloidosis, and Waldenström macroglobulinemia/lymphoplasmacytic lymphoma.[3,4,5]

Ixazomib Citrate: Definitions

- **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.

Ixazomib Citrate: Policy

Note: Coverage of ixazomib citrate 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.

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

Multiple Myeloma:

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

For **FDA** required criteria coverage:

3. In combination with lenalidomide and dexamethasone for patients who have received at least one prior line of therapy[2]; OR

For **NCCN** required criteria coverage:

4. As a substitute for bortezomib or carfilzomib in regimens when given as primary treatment or when used for disease relapse after 6 months following primary induction therapy with the same regimen for non-transplant candidates in select patients for intolerance/logistical reasons; OR
5. Single agent maintenance therapy for one of the following:
   a) Symptomatic disease after response to primary therapy in transplant candidates
   b) Response or stable disease following autologous hematopoietic cell transplant (HCT)
   c) Response or stable disease following either a tandem autologous or allogeneic (HCT) for high-risk patients; OR
6. Relapse or progressive disease previously treated in combination with one of the following:
   a) Dexamethasone and pomalidomide for patients who have received two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy, if lenalidomide - or anti-CD-38-refractory regimen
   b) Dexamethasone and lenalidomide
   c) Cyclophosphamide and dexamethasone
   d) Venetoclax and dexamethasone for patients with the chromosomal translocation t(11:14).[3]

Systemic Light Chain Amyloidosis

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

For **NCCN** required criteria coverage:

3. Relapsed or refractory previously treated disease in combination with one of the following:
   a) Dexamethasone
   b) Dexamethasone and lenalidomide
   c) Dexamethasone and cyclophosphamide.[4]

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma

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

For **NCCN** required criteria coverage:

3. In combination with rituximab and dexamethasone for one of the following:
   a) Primary therapy
   b) Relapse disease if previously used as primary therapy that was well tolerated and elicited a prolonged response
   c) Alternative therapy for previously treated disease with persistent symptoms following primary therapy or that does not respond to primary therapy or for progressive or relapsed disease.[5]

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

Ixazomib Citrate: References

1. Hematol et al. The potential of ixazomib, a second-generation proteasome inhibitor, in the treatment of multiple myeloma. https://pmc.ncbi.nlm.nih.gov/articles/PMC5495505/. Accessed December 18, 2024.
2. Ixazomib (Ninlaro) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208462s017lbl.pdf. Accessed December 18, 2024.
3. National Comprehensive Cancer Network. Multiple Myeloma. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed December 18, 2024.
4. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis. https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed December 18, 2024.
5. National Comprehensive Cancer Network. Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma. https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed December 18, 2024.

Ixazomib Citrate: 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
C88.0	Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
C90.0	Multiple myeloma
C9399, J8999	Ixazomib citrate
E85.81	Systemic light chain amyloidosis

Ixazomib Citrate: 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:	