PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral – Proteasome Inhibitor) – Ninlaro Prior Authorization Policy
- Ninlaro® (ixazomib capsules – Takeda)

REVIEW DATE: 04/15/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Ninlaro, an oral proteasome inhibitor, is indicated in combination with lenalidomide and dexamethasone for the treatment of **multiple myeloma** in patients who have received at least one prior therapy.[1]

Limitations of Use: Ninlaro is not recommended for use in the maintenance setting or in newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone outside of controlled clinical trials.

Guidelines

Ninlaro is discussed in in the National Comprehensive Cancer Network (NCCN) guidelines:

- **Multiple Myeloma:** NCCN guidelines (version 5.2026 – January 9, 2025) list multiple therapeutic regimens that may be used for primary therapy and

previously treated multiple myeloma.[2] For primary therapy for non-transplant candidates, Ninlaro may be substituted for Kyprolis® (carfilzomib intravenous infusion) or bortezomib in select patients in case of intolerance/logistical reasons (category 2A). In this setting, Ninlaro/lenalidomide/dexamethasone is also recommended (category 2A). For maintenance therapy, Ninlaro monotherapy is listed under "Useful in Certain Circumstances" after autologous or allogeneic hematopoietic cell transplant candidates (category 2B). Ninlaro is also recommended as maintenance therapy after response to primary myeloma therapy in transplant candidates (category 2A). For previously treated disease that has relapsed or is refractory after one to three prior therapies, Ninlaro/lenalidomide/dexamethasone (category 1) or Ninlaro/cyclophosphamide/dexamethasone (category 2A) are recommended as "Other Recommended Regimens"; Venclexta® (venetoclax tablets)/dexamethasone/Ninlaro is recommended only for t(11;14) patients as "Useful in Certain Circumstance." Ninlaro/pomalidomide/dexamethasone is recommended after two prior therapies including an immunomodulatory agent and a proteasome inhibitor with disease progression on or within 60 days of completion of last therapy; this regimen is "Preferred" for anti-CD-38 refractory or lenalidomide-refractory patients.

- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2026 – March 16, 2026) list Ninlaro/cyclophosphamide/dexamethasone, Ninlaro/ /dexamethasone ± lenalidomide among the treatment options for patients with previously treated disease (all category 2A).[3]
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 2.2026 – March 3, 2026) list Ninlaro/rituximab/dexamethasone among the treatment options for primary therapy and for previously treated disease (category 2A).[4]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Ninlaro. All approvals are provided for the duration noted below.

- **Ninlaro® (ixazomib capsules – Takeda)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Multiple Myeloma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i, ii, iii, or iv):
      i. Ninlaro will be taken in combination with lenalidomide or cyclophosphamide and dexamethasone; OR
      ii. Patient has received at least one prior regimen for multiple myeloma; OR

Note: Examples include regimens containing bortezomib, cyclophosphamide, Kyprolis (carfilzomib intravenous infusion), lenalidomide, Darzalex (daratumumab intravenous infusion).

iii. The medication will be used following hematopoietic stem cell transplantation; OR

iv. Patient meets BOTH of the following (a and b):

a) According to the prescriber, the patient is not a candidate for bortezomib or Kyprolis (carfilzomib intravenous infusion); AND

b) Patient is not a transplant candidate.

Other Uses with Supportive Evidence

2. **Systemic Light Chain Amyloidosis.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one other regimen for this condition.
   Note: Examples of agents used in other regimens include Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), Kyprolis (carfilzomib intravenous infusion), bortezomib, lenalidomide, cyclophosphamide, and melphalan.

3. **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is used in combination with a rituximab product and dexamethasone.

CONDITIONS NOT COVERED

- **Ninlaro® (ixazomib capsules – Takeda)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Ninlaro® capsules [prescribing information]. Cambridge, MA: Takeda; July 2024.
2. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 5.2026 – January 9, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 9, 2026.
3. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2026 – March 16, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 9, 2026.
4. The NCCN Waldenstrom Macroglobulinemia/Lymphoblastic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2026 – March 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 9, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/24/2024

Annual Revision	**Multiple Myeloma:** The criterion that "the medication will be used following autologous stem cell transplantation (ASCT)" was changed to, "the medication will be used following hematopoietic stem cell transplantation." **Systemic Light Chain Amyloidosis:** Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), and Kyprolis (carfilzomib intravenous infusion) were added to the Note as examples of agents used in other regimens.	04/09/2025
Update	04/11/2025: The policy name was changed from "Oncology – Ninlaro PA Policy" to "Oncology (Oral – Proteasome Inhibitor) – Ninlaro PA Policy".	N/A
Selected Revision	**Multiple Myeloma:** An option for approval was added, which states that "according to the prescriber, the patient is not a candidate for bortezomib or Kyprolis (carfilzomib intravenous infusion) and patient is not a transplant candidate."	05/14/2025
Annual Revision	No criteria changes.	04/15/2026