PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 04/12/2023

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. 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 treatment of patients with **multiple myeloma** 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. Ninlaro should be taken once a week on the same day and at approximately the same time for the first 3 weeks of a 4-week cycle. There are dose modification guidelines which are recommended to manage treatment-related adverse events, including platelet count, absolute neutrophil count (ANC), and other toxicities (e.g., rash, peripheral neuropathy). Treatment should be continued until disease progression or unacceptable toxicity. Safety and efficacy are not established in patients < 18 years of age.

Guidelines

Ninlaro is discussed in various guidelines from the National Comprehensive Cancer Network (NCCN).

- **Multiple Myeloma:** NCCN guidelines (version 3.2023 – December 8, 2022) list multiple therapeutic regimens that may be used for primary therapy and previously treated multiple myeloma.[2] For primary therapy, in transplant

candidates, Ninlaro/cyclophosphamide/dexamethasone (category 2A) and Ninlaro/lenalidomide/dexamethasone (category 2B) are listed under "Useful in certain circumstances". Ninlaro/lenalidomide/dexamethasone is a category 2A recommendation for non-transplant candidates under "Other recommended regimens". Maintenance with Ninlaro is also listed among the alternatives for transplant and non-transplant candidates (category 2B for both settings). For previously treated disease, multiple regimens are listed, including Ninlaro/lenalidomide/dexamethasone (preferred, category 1), Ninlaro/Pomalyst (pomalidomide capsules)/dexamethasone (preferred for "Bortezomib-refractory" group), and Ninlaro/cyclophosphamide/dexamethasone under "Other recommended regimens for early relapses (1-3 prior therapies).

- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2022 – November 28, 2022) list Ninlaro ± dexamethasone and Ninlaro/lenalidomide/dexamethasone among the treatment options for patients with previously treated disease (both category 2A).[3]
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 1.2023 – July 6, 2022) list Ninlaro/rituximab/dexamethasone (category 2A) among the treatment options for primary therapy and for previously treated disease.[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, or iii):
     - **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 autologous stem cell transplantation (ASCT).

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 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 experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Ninlaro® capsules [prescribing information]. Cambridge, MA: Takeda; April 2022.
2. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2023 – December 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 30, 2023.
3. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2023 – November 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 30, 2023.
4. The NCCN Waldenstrom Macroglobulinemia/Lymphoblastic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – July 6, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 30, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/06/2022
Selected Revision	Approval durations were changed from 3 years to 1 year.	06/22/2022
Annual Revision	**Multiple Myeloma:** In reference to Ninlaro combination therapy, added "or cyclophosphamide."	04/12/2023