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| **Section:** | Prescription Drugs | **Effective Date:** | July 1, 2022 |
| **Subsection:** | Antineoplastic Agents | **Original Policy Date:** | December 11, 2015 |
| **Subject:** | Ninlaro | **Page:** | 1 of 5 |

***Last Review Date:*** June 16, 2022

# Ninlaro

## Description

Ninlaro (ixazomib)

**Background**
Ninlaro is the first oral proteasome inhibitor approved to treat multiple myeloma in patients who have received at least one prior therapy. Ninlaro is to be used in combination with Revlimid (lenalidomide), an immunomodulator, and dexamethasone, an anti-inflammatory medication. Multiple myeloma causes plasma cells to rapidly multiply and crowd out other healthy blood cells from the bone marrow. When the bone marrow has too many plasma cells, the cells may move to other parts of the body. Ninlaro works by blocking enzymes, known as 20S proteasomes, from multiple myeloma cells and hinder their ability to grow and survive. Ninlaro should be taken once a week on the same day and approximately the same time for the first 3 weeks of the 4 week cycle. Treatment should be continued until disease progression or unacceptable toxicity (1).

**Regulatory Status**
FDA-approved indication: Ninlaro is a proteasome inhibitor indicated in combination with lenalidomide and dexamethasone for the 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 (1).

Off-Label Use: (2-3)

1. Relapsed or refractory multiple myeloma (MM) - used in combination with dexamethasone.

Patients should be monitored for thrombocytopenia, gastrointestinal toxicities, peripheral neuropathy, peripheral edema, cutaneous reactions, hepatotoxicity, and embryo-fetal toxicity. Platelet counts and absolute neutrophil counts should be monitored at baseline, at least monthly during treatment, and more frequently during the first three cycles of Ninlaro. The most common laboratory abnormalities were low platelets (thrombocytopenia) and low absolute neutrophil count (neutropenia). Women should avoid getting pregnant while on this medication (1).

The safety and efficacy of Ninlaro in children has not been established (1).

**Related policies**
Kyprolis, Velcade

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Ninlaro may be considered **medically necessary** in patients 18 years of age or older with multiple myeloma and if the conditions indicated below are met.

Ninlaro may be considered **investigational** for patients that are less than 18 years of age and for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)
    a. Used in combination with Revlimid (lenalidomide) and dexamethasone

2. Relapsed, progressive or refractory multiple myeloma (MM)
    a. Used in combination with dexamethasone

**AND ALL** of the following:
a. Patient had at least one prior multiple myeloma therapy
b. **NO** dual therapy with another proteasome inhibitor

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)
    a. Used in combination with Revlimid (lenalidomide) and dexamethasone

2. Relapsed, progressive or refractory multiple myeloma (MM)
    a. Used in combination with dexamethasone

**AND ALL** of the following:
a. **NO** unacceptable toxicities
b. **NO** dual therapy with another proteasome inhibitor

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Duration** 6 months

### Prior – Approval *Renewal* Limits

**Duration** 12 months

## Rationale

**Summary**

Ninlaro is the first oral proteasome inhibitor approved to treat multiple myeloma in patients who have received at least one prior therapy. Ninlaro is to be used in combination with Revlimid (lenalidomide), an immunomodulator, and dexamethasone, an anti-inflammatory medication. Women should avoid getting pregnant while on this medication. The safety and efficacy of Ninlaro in children has not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Ninlaro while maintaining optimal therapeutic outcomes.

**References**

1. Ninlaro [package insert]. Cambridge, MA: Takeda Pharmaceutical Company Limited; April 2022.
2. NCCN Drugs & Biologics Compendium® Ixazomib 2022. National Comprehensive Cancer Network, Inc. Accessed on April 13, 2022.
3. NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 5.2022). National Comprehensive Cancer Network, Inc. March 2022. Accessed on April 13, 2022.

## Policy History

| Date | Action |
|---|---|
| December 2015 | Addition to PA |
| March 2016 | Annual review<br>Policy number changed from 5.04.71 to 5.21.71 |
| June 2016 | Annual editorial review and reference update<br>Added diagnosis relapsed, progressive or refractory multiple myeloma (MM); used in combination with dexamethasone. |
| September 2016 | Annual review |
| June 2017 | Annual review and reference update |
| June 2018 | Annual editorial review and reference update |
| June 2019 | Annual review and reference update |
| June 2020 | Annual review and reference update |
| December 2020 | Annual review |
| September 2021 | Annual review and reference update |
| June 2022 | Annual editorial review and reference update. Added limitations of use statement per PI update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.**