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5.21.071

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 11, 2015
Subject:	Ninlaro	**Page:**	1 of 5

Last Review Date: March 7, 2025

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 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 effectiveness of Ninlaro in pediatric patients less than 18 years of age have 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** if the conditions indicated below are met.

Ninlaro may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. 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

Diagnosis

Patient must have the following:

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

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. **NO** dual therapy with another proteasome inhibitor

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

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 dexamethasone, an anti-inflammatory medication. Female patients should avoid getting pregnant while on this medication. The safety and effectiveness of Ninlaro in pediatric patients less than 18 years of age have 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; July 2024.
2. NCCN Drugs & Biologics Compendium® Ixazomib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 13, 2025.
3. NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2025). National Comprehensive Cancer Network, Inc. September 2024. Accessed on January 13, 2025.

Policy History

Date	Action
December 2015	Addition to PA
March 2016	Annual review Policy number changed from 5.04.71 to 5.21.71
June 2016	Annual editorial review and reference update 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
October 2022	Revised requirements for clarity: combined diagnoses and removed requirement for MM to be used in combination with lenalidomide. Revised renewal requirement to “no disease progression or unacceptable toxicity” for consistency. Changed approval duration to 12 months. Changed policy number to 5.21.071
December 2022	Annual review and reference update
March 2023	Annual review and reference update
December 2023	Annual review and reference update
June 2024	Annual review and reference update

March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.