Ninlaro

(ixazomib)

New Product Slideshow

MPR

Introduction

- **Brand name:** Ninlaro
- **Generic name:** Ixazomib
- **Pharmacological class:** Proteasome inhibitor
- **Strength and Formulation:** 2.3mg, 3mg, 4mg; gel caps
- **Manufacturer:** Takeda
- **How supplied:** Blister pack—1, 3
- **Legal Classification:** Rx

NINLARO


NINLARO
2.3mg
NDC 63020-078-02
℞ only
NINLARO®
(ixazomib) capsules
2.3mg
Contains 3 Packs
(each pack holds 1 capsule)
Takeda
NDC 63020-080-02
NINLARO®
(ixazomib) capsules
4mg
Contains 3 Packs
Takeda
NINLARO
3mg
NDC 63020-079-02
NINLARO®
(ixazomib) capsules
3mg
Contains 3 Packs
Takeda

Indications

- In combination with lenalidomide and dexamethasone for the treatment of patients with **multiple myeloma** who have received at least 1 prior therapy

Dosage & Administration

- Swallow whole
- Take ≥1hr before or ≥2hrs after food
- Initially 4mg once weekly on Days 1, 8, and 15 of a 28-day cycle; continue until disease progression or unacceptable toxicity
- Give with lenalidomide 25mg daily on Days 1–21 and dexamethasone 40mg on Days 1, 8, 15, and 22

Dosage & Administration

- Moderate or severe hepatic impairment, severe renal impairment, or ESRD on dialysis: initially 3mg
- Prior to new cycle, ensure ANC $\geq 1{,}000/mm^3$, platelets $\geq 75{,}000/mm^3$, recovery of non-hematologic toxicities to baseline or Grade ≤ 1
- Dose modifications: see full labeling

Considerations for Special Populations

- **Pregnancy:** avoid
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Geriatric:** No overall differences
- **Renal impairment:** Severe impairment or ESRD: reduce starting dose
- **Hepatic impairment:** Moderate or severe impairment: reduce starting dose

Warnings/Precautions

- **Thrombocytopenia**: monitor platelets at least monthly during treatment; consider more frequently for first 3 cycles
- Adjust dose for Grade 3/4 **GI symptoms** or Grade ≥2 **rash**
- Monitor for **peripheral neuropathy**; adjust dose if worsens.
- Adjust dosing of dexamethasone or ixazomib if Grade 3/4 **peripheral edema** symptoms occur

Warnings/Precautions

- Hepatic impairment: **monitor enzymes** regularly and adjust for Grade 3/4 symptoms
- Severe renal impairment or ESRD
- Males and females of reproductive potential must use **effective contraception** during therapy and for 90 days after final dose

Interactions

- Avoid concomitant strong **CYP3A inducers** (eg, rifampin, phenytoin, carbamazepine, St. John's Wort)

Adverse Reactions

- Diarrhea
- Constipation
- Thrombocytopenia
- Peripheral neuropathy
- Nausea
- Peripheral edema
- Vomiting
- Back pain

Mechanism of Action

- Ixazomib, a **reversible proteasome inhibitor**, exerts its action by preferentially binding and inhibiting the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome
- *In vitro*, ixazomib **induces apoptosis** of multiple myeloma cell lines and demonstrates cytotoxic activity against myeloma cells from patients who had relapsed after multiple prior therapies, including bortezomib, lenalidomide, and dexamethasone
- The combination of ixazomib with lenalidomide demonstrates **synergistic cytotoxic effects** in multiple myeloma cell lines

Pharmacokinetics

- **Distribution:** 99% bound to plasma proteins
- **Metabolism:** Multiple CYP enzymes; no specific CYP isozyme predominantly contributes to metabolism
- **Elimination:** Renal, fecal

Clinical Trials

- The efficacy and safety of Ninlaro in combination with lenalidomide and dexamethasone was evaluated in a randomized, double-blind, placebo-controlled, multicenter study in 722 patients with relapsed and/or refractory multiple myeloma who had received ≥1 prior line of therapy

- Patients who were refractory to lenalidomide or proteasome inhibitors were excluded from the study

Clinical Trials

- Patients were randomized 1:1 to receive either the combination of Ninlaro 4mg (Days 1, 8, and 15), lenalidomide 25mg (Days 1–21), and dexamethasone 40mg (Days 1, 8, 15, and 22) (n=360) or the combination of placebo, lenalidomide and dexamethasone (n=362) on the same schedule of a 28-day cycle until disease progression or unacceptable toxicities

- The efficacy outcome measure was **progression-free survival** (PFS) according to the 2011 IMWG response criteria as assessed by a blinded independent review committee (IRC) based on central lab results

Clinical Trials

- Patients treated with the Ninlaro regimen demonstrated **statistically significant improvement** in PFS vs. the placebo regimen (HR 0.74, [95% CI: 0.59, 0.94]; *P*=0.012)

- The median **PFS** for the Ninlaro regimen was **20.6 months** vs. the placebo regimen at **14.7 months**

Clinical Trials

- The median **time to response** and median **duration of response** were 1.1 months and 20.5 months in the Ninlaro regimen vs. 1.9 months and 15 months in the placebo regimen, respectively

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the complete product monograph available at:

http://www.empr.com/ninlaro/drugproduct/414/