

NINLARO® (ixazomib) Treatment Guide


NINLARO is a prescription medicine used to treat multiple myeloma in combination with the medicines REVLIMID® (lenalidomide) and dexamethasone, in people who have received at least one prior treatment for their multiple myeloma.

NINLARO should not be used to treat the following people, unless they are participants in a controlled clinical trial:

- people who are receiving maintenance treatment, or
- people who have been newly diagnosed with multiple myeloma.

It is not known if NINLARO is safe and effective in children.

Please read the Important Safety Information on pages 8-9 and the Patient Information in the accompanying NINLARO (ixazomib) full Prescribing Information.

 **NINLARO®**
(ixazomib) capsules
4mg | 3mg | 2.3mg

I have a phenomenal team of doctors and we've worked together to develop a treatment plan that's right for me.

Visit www.NINLARO.com to get helpful information about NINLARO® (ixazomib) and tools for taking NINLARO and keeping track of your schedule.

Welcome to the NINLARO Treatment Guide

This booklet provides important information about NINLARO, organized into tabbed sections.

- **What Is NINLARO** describes the medication and tells you how it works
- **How NINLARO Can Help** explains the benefits and effectiveness of the NINLARO regimen (NINLARO+lenalidomide+dexamethasone)
- **Important Safety Information and Side Effects** describes the side effects associated with treatment and some tips that have been recommended to help manage them
- **How To Take NINLARO** discusses the dosing schedule for the NINLARO regimen

For more information about NINLARO, visit www.NINLARO.com.

"When my doctor brought up the NINLARO regimen as an appropriate option for me, I wanted to learn more because it is an all-oral option that I could take at home."

Please read the Important Safety Information on pages 8-9 and the [Patient Information in the accompanying NINLARO \(ixazomib\) full Prescribing Information](#).

What is NINLARO® (ixazomib)?

NINLARO is a prescription medicine used to treat multiple myeloma in combination with the medicines REVLIMID® (lenalidomide) and dexamethasone, in people who have received at least 1 prior treatment for their multiple myeloma. NINLARO should not be used in patients with newly diagnosed multiple myeloma or as a maintenance treatment unless they are part of a trial. It is not known if NINLARO is safe and effective in children.

NINLARO belongs to a family of anticancer drugs called proteasome inhibitors that treat multiple myeloma. Myeloma is a cancer of the plasma cells.

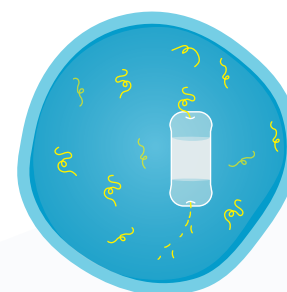
NINLARO is the first proteasome inhibitor available in a capsule for multiple myeloma. This is an anticancer medicine that you can take at home or wherever is convenient for you. That may mean less time at the clinic and more time to focus on other things in your life, such as family and friends.

"My doctor said I was a good candidate for the NINLARO regimen and we discussed the risks and benefits I could experience with NINLARO."

Please read the Important Safety Information on pages 8-9 and the Patient Information in the accompanying NINLARO (ixazomib) full Prescribing Information.

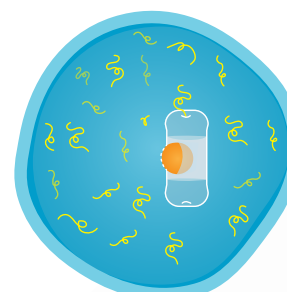
How NINLARO works

Myeloma cell



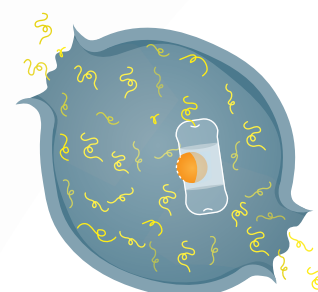
- Proteasomes are inside cells
- They act like garbage disposals, digesting unneeded or damaged proteins within cells
- Myeloma cells are more dependent on proteasomes than normal cells

Proteasome inhibition



- NINLARO is the **first oral proteasome inhibitor**
- It targets the proteasomes inside cells, slowing down or blocking the proteasomes from digesting and discarding the proteins within cells

Cell death



- As the proteasome is unable to digest the additional proteins within cells, a buildup of proteins begins to develop
- The buildup of proteins within cells can lead to cell death

 Myeloma cell
  Protein
  NINLARO
  Proteasome
  Digested protein

How NINLARO® (ixazomib) can help

NINLARO has been proven in a study to help some patients live longer without their multiple myeloma getting worse.*

In a study of NINLARO, the NINLARO regimen was proven to work in some people whose multiple myeloma had come back or stopped responding to prior therapy.

This study evaluated progression-free survival (PFS), the length of time during and after treatment that a patient lives with multiple myeloma but it does not get worse. The study also looked at other measurements, including overall survival and time to response.

NINLARO is approved for treatment until the disease worsens or the treatment is no longer tolerated.

Treatment with the NINLARO regimen increased the median progression-free survival by about 6 months.

20.6 MONTHS with NINLARO regimen

14.7 MONTHS with placebo regimen

Overall survival

In this study, the overall survival of patients who received the NINLARO regimen was similar to that of patients who received the placebo regimen.



Study setup†

One group of study patients was given the **NINLARO regimen**.

- NINLARO and 2 other drugs used to treat multiple myeloma: REVLIMID® (lenalidomide) and dexamethasone
- All 3 medicines work together (also called a triplet regimen) to fight the cancer



For comparison, another group of patients was given the **placebo regimen**.

- Placebo (an inactive pill), REVLIMID (lenalidomide), and dexamethasone

*The US Food and Drug Administration approved NINLARO based on the results of a clinical study. This study tested the NINLARO regimen (NINLARO+lenalidomide+dexamethasone) compared with a placebo regimen (placebo+lenalidomide+dexamethasone) in 722 people whose multiple myeloma had come back or stopped responding to prior therapy. It measured the length of time a patient lived without their disease getting worse.

†In this study, patients were randomly assigned to a study group. Study reviewers did not know which patients received which medication and did not know whose results they were reviewing (called double blind) to give the best objective judgment.

NINLARO was proven to work quickly and effectively



Fast response

- In the NINLARO study, the median time that patients experienced their first response was about **1 month** with the NINLARO regimen compared with a median of about **2 months** with the placebo regimen. It took longer for some patients to see a response



Effective results

- The **majority** of people in the study responded to treatment with NINLARO+lenalidomide+dexamethasone

What does it mean?

Median is the middle number in a set of numbers. For example, a median of 20 months means 50% of the group had more than 20 months and 50% of the group had less than 20 months.

Placebo is an inactive pill, often called a “sugar pill,” that may be given in clinical trials to compare the effects to the active drug.

Respond or response is when the cancer cells decrease after treatment, which shows up as improvement in the laboratory tests that measure the disease, such as blood tests showing a decrease of M protein in multiple myeloma.

Please refer to the glossary in the Treatment Planner or visit NINLARO.com for definitions of medical terms you may not be familiar with.

Remember that it’s important to discuss your treatment with your healthcare provider. Learn more about side effects with NINLARO in the Important Safety Information and Side Effects tab.

Please read the Important Safety Information on pages 8-9 and the Patient Information in the accompanying NINLARO (ixazomib) full Prescribing Information.

IMPORTANT SAFETY INFORMATION FOR NINLARO® (ixazomib)

NINLARO may cause serious side effects, including:

- **Low platelet counts (thrombocytopenia)** are common with NINLARO and can sometimes be serious. You may need platelet transfusions if your counts are too low. Tell your healthcare provider if you have any signs of low platelet counts, including bleeding and easy bruising.
- **Stomach and intestinal (gastrointestinal) problems.** Diarrhea, constipation, nausea, and vomiting are common with NINLARO and can sometimes be severe. Call your healthcare provider if you get any of these symptoms and they do not go away during treatment with NINLARO. Your healthcare provider may prescribe medicine to help treat your symptoms.
- **Nerve problems** are common with NINLARO and may also be severe. Tell your healthcare provider if you get any new or worsening symptoms including: tingling, numbness, pain, a burning feeling in your feet or hands, or weakness in your arms or legs.
- **Swelling** is common with NINLARO and can sometimes be severe. Tell your healthcare provider if you develop swelling in your arms, hands, legs, ankles, or feet, or if you gain weight from swelling.
- **Skin reactions.** Rashes are common with NINLARO. NINLARO can cause rashes and other skin reactions that can be serious and can lead to death. Tell your healthcare provider right away if you get a new or worsening rash, severe blistering or peeling of the skin, or mouth sores.
- **Thrombotic microangiopathy (TMA).** This is a condition involving blood clots and injury to small blood vessels that may cause harm to your kidneys, brain, and other organs, and may lead to death. Get medical help right away if you get any of the following signs or symptoms during treatment with NINLARO: fever, bruising, nose bleeds, tiredness, or decreased urination.
- **Liver problems.** Tell your healthcare provider if you get these signs of a liver problem: yellowing of your skin or the whites of your eyes; pain in your right upper-stomach area.

Other common side effects of NINLARO include low white blood cell counts and bronchitis.

Tell your healthcare provider if you get new or worsening signs or symptoms of the following during treatment with NINLARO:

- skin rash and pain (shingles) due to reactivation of the chicken pox virus (herpes zoster)
- blurred vision or other changes in your vision, dry eye, and pink eye (conjunctivitis)

These are not all the possible side effects of NINLARO. Talk to your healthcare provider for medical advice about side effects. **You may report side effects to Takeda at 1-844-217-6468 or FDA at 1-800-FDA-1088.**

Before taking NINLARO, tell your healthcare provider about all your medical conditions, including if you:

- have liver problems.
- have kidney problems or are on dialysis.
- are pregnant or plan to become pregnant. NINLARO can harm your unborn baby.
- **Females who are able to become pregnant:**
 - Avoid becoming pregnant during treatment with NINLARO.
 - Your healthcare provider will do a pregnancy test before you start treatment with NINLARO.
 - You should use effective non-hormonal birth control during treatment and for 90 days after your last dose of NINLARO. If using hormonal contraceptives (for example, birth control pills), you should also use an additional barrier method of contraception (for example, diaphragm or condom). Talk to your healthcare provider about birth control methods that may be right for you during this time.
 - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with NINLARO.
- **Males with female partners who are able to become pregnant:**
 - You should use effective birth control during treatment and for 90 days after your last dose of NINLARO.
 - Tell your healthcare provider right away if your partner becomes pregnant or thinks she may be pregnant while you are being treated with NINLARO.
- are breastfeeding or plan to breastfeed. It is not known if NINLARO passes into breast milk, if it affects an infant who is breastfed, or breast milk production. Do not breastfeed during treatment with NINLARO and for 90 days after your last dose of NINLARO.

IMPORTANT SAFETY INFORMATION FOR NINLARO (cont'd)

Taking too much NINLARO (overdose) can cause serious side effects, including death. If you take more NINLARO than instructed by your healthcare provider, call your healthcare provider right away or go to the nearest hospital emergency room right away. Take your medicine pack with you.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements or before starting any new medicines. Talk to your healthcare provider before starting any new medicines during treatment with NINLARO.

Please read the Patient Information in the accompanying NINLARO (ixazomib) full Prescribing Information.

Side effect management

Side effects may occur while on treatment with NINLARO. Talk with your healthcare provider about your side effects. Consider keeping a diary of how you are feeling to help in your discussions with your healthcare provider.

The side effects discussed below can give you an understanding of what may be commonly encountered during treatment. The guidance given can serve as a talking point for your conversations with your healthcare team about side effects.

These recommendations come from healthcare professionals who have worked with patients with various cancers. These are not meant to replace medical advice from your healthcare provider.

Immediately report any side effect to your healthcare team. Always consult with your healthcare provider before taking any action.

Nausea and vomiting

- Make sure you let your healthcare team know when you experience nausea or vomiting so they can help you best manage your symptoms
- There are many ways to manage nausea/vomiting, including lifestyle changes such as changing some things you eat or drink. Ask your healthcare team for recommendations
- Your healthcare provider may also give you a medication to prevent or treat nausea
 - Let your healthcare team know if the medicines for nausea/vomiting aren't working. You may have to try a few different medicines to find the one that works best for you

Constipation

- After talking with your healthcare provider, you may be asked to modify your diet to include more liquids or change to certain foods to reduce constipation
- Exercise may also be recommended. Always consult with your healthcare team if a certain exercise regimen is appropriate for you
- Your healthcare provider may prescribe a laxative or other medicine

Diarrhea

- Ask your healthcare team for specific recommendations for coping with diarrhea
- You may be asked to eat certain foods and make changes to your overall diet
- You may be advised to drink fluids to stay hydrated
- Your healthcare provider may give you medicines to reduce the diarrhea

Rash



- It is important to immediately report rash or any skin changes to your healthcare team
- Do not diagnose or treat yourself to avoid making the rash worse


"My doctor went over all the side effects of NINLARO, that was really important to me."


How to take NINLARO® (ixazomib)


NINLARO is a capsule that you take once a week for 3 weeks, followed by 1 week off. NINLARO is taken with 2 other medications, REVLIMID® (lenalidomide) and dexamethasone, in 4-week cycles. This dosing calendar is a snapshot of the NINLARO regimen for a 28-day (4-week) cycle. Talk to your doctor about dosing for these medications.

Taking too much NINLARO (overdose) can cause serious side effects, including death. If you take more NINLARO than instructed by your healthcare provider, call your healthcare provider immediately or go to the nearest hospital emergency room right away. Take your medicine pack with you.

WEEK	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
1							
2							
3							
4		NO DOSE	NO DOSE	NO DOSE	NO DOSE	NO DOSE	NO DOSE

 NINLARO
(4 mg, 3 mg, 2.3 mg)

 Lenalidomide
(25 mg)

 Dexamethasone
(40 mg)

Additional dosing information

- Take each dose of NINLARO at about the **same time of day**
- Take NINLARO **at least 1 hour before eating or at least 2 hours after food**
 - Food may interfere with the absorption of NINLARO, which may lower levels of the medication in the blood and possibly reduce effectiveness
- Swallow the capsule **whole with water**. Do not chew, open, crush, or break the capsule
- If you miss a dose of NINLARO you can take the missed dose as long as the next scheduled dose is **3 or more days away**
- If you vomit after taking a dose, **do not repeat the dose**. Even if you vomit after a dose, your body may have taken in some of the medication. Instead, take your next dose of NINLARO on the next scheduled day and time
- If you **take more NINLARO than you were prescribed**, call your healthcare provider right away or go to the nearest hospital emergency room

"It's important to work with your healthcare team and follow their guidance."

Please read the Important Safety Information on pages 8-9 and the Patient Information in the accompanying NINLARO (ixazomib) full Prescribing Information.

I was eager to try the
NINLARO® (ixazomib)
regimen because it
meant I could take my
medication at home.



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