Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a physician's prescription only

Ninlaro® 2.3 mg
Ninlaro® 3 mg
Ninlaro® 4 mg

Capsules

Active ingredient:

Each capsule of Ninlaro® 2.3 mg contains 2.3 mg of ixazomib (equivalent to 3.3 mg of ixazomib citrate).

Each capsule of Ninlaro® 3 mg contains 3 mg of ixazomib (equivalent to 4.3 mg of ixazomib citrate).

Each capsule of Ninlaro® 4 mg contains 4 mg of ixazomib (equivalent to 5.7 mg of ixazomib citrate).

Inactive ingredients and allergens in this medicine: See section 6 "Additional information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your physician or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

This medicine is intended for adults.

1. What is this medicine intended for?

Ninlaro in combination with lenalidomide and dexamethasone is indicated for the treatment of patients with multiple myeloma (a type of cancer of the bone marrow) who have received at least one prior therapy.

Therapeutic group: Antineoplastic agent of proteasome inhibitor class.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any other ingredients that this medicine contains (see section 6: "Additional information").

Special warnings about using this medicine

Before using Ninlaro, tell your physician about your medical condition, including if:

- you suffer from liver problems
- you suffer from kidney problems or are on dialysis
- you are pregnant or plan to become pregnant (see additional details under "Pregnancy and breastfeeding")
- you are breastfeeding or plan to breastfeed (see additional details under "Pregnancy and breastfeeding")

Tell your physician if you get new or worsening signs and 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 conjunctivitis (eye infection)

Children and adolescents:

There is no information about the safety and efficacy of using this medicine in children and adolescents.

Tests and follow-up

Your physician will refer you for blood tests during the period of treatment with the medicine, in order to monitor side effects.

Drug interactions

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your physician or pharmacist.
Tell your physician or pharmacist before starting any new medicines during treatment with Ninlaro.
In particular, tell your physician or pharmacist if you are taking medicines belonging to a group of medicines called "strong CYP3A inducers" (such as rifampin, phenytoin, carbamazepine and hypericum (St. John's Wort)).

Using the medicine and food

- **Take Ninlaro at least one hour before or at least two hours after food**
- **On days that you take both Ninlaro and dexamethasone, do not** take both medications at the same time. **Take dexamethasone with food.**

Pregnancy and breastfeeding

Pregnancy
- Ninlaro can harm your unborn baby.
    - Avoid becoming pregnant during treatment with Ninlaro.
    - Your physician will refer you for a pregnancy test before you start treatment with Ninlaro.
    - Men and women of childbearing potential must use effective contraception during treatment with Ninlaro and for 3 months (90 days) after the end of treatment. You should use effective non-hormonal contraception. If using hormonal contraceptives (for example, the pill), you must also use an additional barrier method of contraception (for example, diaphragm or condom).
    - Consult your physician about what contraceptives are right for you during treatment.
    - Tell your physician right away in case of pregnancy or suspected pregnancy if you or your partner is being treated with Ninlaro.

Breastfeeding
- It is not known whether 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 3 months (90 days) after the end of treatment.

3. How to use the medicine?

Always use the medicine according to the physician's instructions. Check with your physician or pharmacist if you are not sure about your dose or about how to take this medicine. Only your physician will determine your dose and how you should take this medicine.

Ninlaro is taken in treatment cycles. Each cycle lasts 4 weeks (28 days). The recommended dose is usually:

one Ninlaro 4 mg capsule once a week on the same day of the week and at about the same time of day, for **the first 3 weeks** of a 4-week cycle (taken on days 1, 8 and 15 of a 28-day treatment cycle).

Take lenalidomide (25 mg) daily for the first 3 weeks of a 4-week cycle (taken on days 1 through 21 of a 28-day treatment cycle).

Take dexamethasone (40 mg) once a week on the same day of each week of a 4-week cycle (taken on days 1, 8, 15 and 22 of a 28-day treatment cycle).

Take lenalidomide and dexamethasone exactly as instructed by your physician; also, be sure to read the relevant patient leaflet and to contact your physician or pharmacist for additional information.

Your physician may adjust your dosages of Ninlaro or of the medications mentioned above, or instruct you to stop them if you experience any side effects, or if you suffer from liver or kidney problems.

Your physician may prescribe a medicine for you to take together with Ninlaro, which reduces the risk that the chicken pox virus (Herpes zoster) will reactivate.

Do not exceed the recommended dose.

- Swallow your Ninlaro capsule whole with water. **Do not** crush, **do not** chew and **do not** open the capsule.
- Avoid direct contact with the capsule contents. If you accidentally get powder from the Ninlaro capsule on your skin, wash the area well with soap and water. If you accidentally get powder from the Ninlaro capsule in your eyes, flush your eyes well with water.
- If you vomit after taking a dose of the medicine, **do not** repeat the dose. Take your next dose of Ninlaro on the next scheduled day and time.

If you have accidentally taken a higher dose of Ninlaro
Taking an overdose of Ninlaro can cause serious side effects, including death. If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, immediately see a physician or go to a hospital emergency room and bring the medicine package with you.

If you forget to take Ninlaro

If you forget to take the medicine or belatedly remember to take a dose of Ninlaro, take the missed dose only if there are more than 3 days (72 hours) before the next scheduled dose. **Do not** take the missed dose if there are 3 days (72 hours) or less before the next scheduled dose.

Adhere to the treatment as recommended by the physician.
Even if your health improves, do not stop taking this medicine without consulting your physician.

If you stop taking Ninlaro
Do not change your dose and do not stop taking Ninlaro without consulting your physician.

Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult the physician or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using Ninlaro may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Ninlaro may cause serious side effects, including:

Low platelet count (thrombocytopenia). Low platelet count is a very common side effect associated with use of Ninlaro (occurred in more than one in 10 users), and can sometimes be serious. You may need platelet transfusions if your count is too low. Tell your physician if you notice any signs of low platelet count, including bleeding and increased tendency to bruise.

Gastrointestinal problems. Diarrhea, constipation, nausea, and vomiting are very common side effects associated with use of Ninlaro (occurred in more than one in 10 users), and can sometimes be severe. Tell your physician if any of these symptoms persist during treatment with Ninlaro. Your physician may decide to prescribe a medicine to help treat these symptoms.

Neurological problems (peripheral neuropathy). Neurological problems are very common side effects associated with use of Ninlaro (occurred in more than one in 10 users), and may also be severe. Tell your physician if you experience new or worsening of one or more of the following symptoms:

- tingling
- numbness
- pain
- a burning feeling in your feet or hands
- weakness in your arms or legs

Peripheral edema. Edema is a very common side effect associated with use of Ninlaro (occurred in more than one in 10 users), and can sometimes be severe. Tell your physician if you develop abnormal swelling of the face, arms, hands, legs, ankles or feet, or if you gain weight from swelling.

Skin reactions. Tell your physician immediately if you develop a new rash or if an existing rash gets worse, severe blistering or peeling of the skin, or mouth sores. Rash is a very common side effect when using Ninlaro (occurred in more than one in 10 users). Ninlaro may cause rashes and other skin reactions that may be serious and may lead to death.

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
- nosebleeds
- tiredness
- decreased urination

Liver problems. Tell your physician if you experience the following symptoms indicating a liver problem. These are common side effects when using Ninlaro (occurred in less than one in 10 users):

- yellowing of the skin or the whites of the eyes
- pain in the right upper stomach area

Additional very common side effects (occurred in more than one in 10 users):

- back pain
- bronchitis
- upper respiratory tract infection (cold-like symptoms)
- eye diseases such as blurred vision, dry eyes and conjunctivitis (eye infection).
- low count of white blood cells called neutrophils (neutropenia) which could increase the risk of infection.

Additional common side effects (occurred in less than one in 10 users):

- skin rash and pain (shingles) as a result of reactivation of the chicken pox virus (herpes zoster).

Serious side effects that are uncommon (occurred in less than one in 1,000 users):

- Sweet's syndrome (acute febrile neutrophilic dermatosis) – acute dermatitis accompanied by fever and increased neutrophil count.
- Stevens-Johnson syndrome – a syndrome in which there is skin blistering and necrosis or mouth sores.
- Transverse myelitis – inflammation of the spinal cord.
- Posterior reversible encephalopathy syndrome.
- Tumor lysis syndrome – a syndrome resulting from rapid destruction of tumor cells and characterized by elevated blood levels of phosphorus and uric acid, reduced levels of calcium, and kidney damage.
- Purpuric rash accompanied by blood clotting and decrease in platelet count (thrombotic thrombocytopenic purpura).

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your physician.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:
https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your physician.

Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

Even if stored as recommended, medicines keep for a limited period only. Please note the expiry date of this medicine! In case of doubt, consult the pharmacist who dispensed the medicine.

Do not store above 30°C. Do not freeze.
Store in the original packaging until just before each use.
Remove the capsule from the blister just before you take it.
Do not throw away the medicine via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient the medicine also contains:
microcrystalline cellulose, talc and magnesium stearate.

Capsule shell and ink contain:
gelatin, titanium dioxide, red iron oxide (Ninlaro 2.3 mg, Ninlaro 4 mg), yellow iron oxide (Ninlaro 4 mg), black iron oxide, shellac, propylene glycol, potassium hydroxide.

What the medicine looks like and contents of the pack:

Ninlaro 2.3 mg gelatin capsules are light pink, with "Takeda" printed on the cap and "2.3 mg" printed on the capsule's body in black ink.
Ninlaro 3 mg gelatin capsules are light grey, with "Takeda" printed on the cap and "3 mg" printed on the capsule's body in black ink.
Ninlaro 4 mg gelatin capsules are light orange, with "Takeda" printed on the cap and "4 mg" printed on the capsule's body in black ink.

Each package of the product contains 3 separate blister trays. Each blister tray contains one capsule.

Name and address of registration holder and importer: Takeda Israel Ltd., 25 Efal St., Petach-Tikva 4951125

This leaflet was revised in September 2024.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

156-81-34609-00
156-82-34615-00
156-83-34616-00