Package leaflet: Information for the patient

NINLARO 2.3 mg hard capsules
NINLARO 3 mg hard capsules
NINLARO 4 mg hard capsules
ixazomib

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What NINLARO is and what it is used for

What NINLARO is
NINLARO is a cancer medicine that contains ixazomib, a 'proteasome inhibitor'.

NINLARO is used to treat a cancer of the bone marrow called multiple myeloma. Its active substance ixazomib works by blocking the action of proteasomes. These are structures inside the cell that digest proteins and are important for cell survival. Because myeloma cells produce a lot of proteins, blocking the action of proteasomes can kill the cancerous cells.

What NINLARO is used for
NINLARO is used to treat adults with multiple myeloma. NINLARO will be given to you together with lenalidomide and dexamethasone, which are other medicines used to treat multiple myeloma.

What multiple myeloma is
Multiple myeloma is a cancer of the blood which affects a type of cell, called the plasma cell. A plasma cell is a blood cell that normally produces proteins to fight infections. People with multiple myeloma have cancerous plasma cells, also called myeloma cells, which can damage the bones. Protein produced by myeloma cells can damage the kidneys. Treatment for multiple myeloma involves killing myeloma cells and reducing the symptoms of the disease.

2. What you need to know before you take NINLARO

Do not take NINLARO
- if you are allergic to ixazomib or to any of the other any of the other ingredients of this medicine (listed in section 6).

If you are uncertain whether the condition above applies to you, talk to your doctor, pharmacist or nurse before taking NINLARO.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking NINLARO if:
- you have a history of bleeding
- you have persistent nausea, vomiting or diarrhoea
- you have a history of nerve problems, to include tingling and numbness
- you have a history of swelling
- you have a persistent rash
- you have or have had liver or kidney problems as your dose may have to be adjusted.

Your doctor will examine you and you will be monitored closely during treatment. Before starting NINLARO and during treatment, you will have blood tests to check that you have enough blood cells.

Children and adolescents
NINLARO is not recommended for use in children and adolescents aged under 18 years.

Other medicines and NINLARO
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This includes any medicines obtained without a prescription, such as vitamins or herbal remedies. This is because other medicines can affect the way NINLARO works. In particular, tell your doctor, pharmacist or nurse if you are taking any of the following medicines: carbamazepine, phenytoin, rifampicin and St. John's wort (*Hypericum perforatum*). These medicines should be avoided as they may reduce the effectiveness of NINLARO.

Pregnancy and breast-feeding
NINLARO is not recommended during pregnancy as it may harm your unborn baby. Breast-feeding should be stopped when taking NINLARO.

Avoid becoming pregnant or breast-feeding while being treated with NINLARO. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

If you are a woman of childbearing potential or a man who can father a child, you must use effective contraception during and for 90 days after treatment. Women using hormonal contraceptives should additionally use a barrier method of contraception. Tell doctor right away if you or your partner becomes pregnant while receiving NINLARO.
As NINLARO is given in combination with lenalidomide, you should adhere to the pregnancy prevention programme of lenalidomide because lenalidomide can be harmful to the unborn child.

See the package leaflets for lenalidomide and dexamethasone for additional information on pregnancy and breast-feeding

Driving and using machines
NINLARO may affect your ability to drive or use machines. You may feel tired and dizzy while taking NINLARO. Do not drive or operate machines if you have these side effects.

3. How to take NINLARO

NINLARO must be prescribed to you by a doctor with experience of treating multiple myeloma. Always take this medicine exactly as your doctor or pharmacist has told you.

NINLARO is used with lenalidomide (a medicine which affects how your immune system works) and dexamethasone (an anti-inflammatory medicine).

NINLARO, lenalidomide and dexamethasone are taken in 4-week treatment cycles. NINLARO is taken once a week (on the same day of the week) for the first 3 weeks of this cycle. The recommended dose is one 4 mg capsule taken by mouth.

The recommended dose of lenalidomide is 25 mg taken every day for the first 3 weeks of the cycle. The recommended dose of dexamethasone is 40 mg taken once a week on the same day for all 4 weeks of the cycle.

Dosing schedule: NINLARO taken with lenalidomide and dexamethasone

✔ Take medicine

28-day cycle (a 4-week cycle)								
	Week 1		**Week 2**		**Week 3**		**Week 4**	
	Day 1	Days 2 to 7	Day 8	Days 9 to 14	Day 15	Days 16 to 21	Day 22	Days 23 to 28
NINLARO	✔		✔		✔			
Lenalidomide	✔	✔ Daily	✔	✔ Daily	✔	✔ Daily		
Dexamethasone	✔		✔		✔		✔	

You should read the Package Leaflets of these other medicines for further information on their use and effects.

If you have liver or kidney problems, your doctor may prescribe NINLARO capsules containing 3 mg. If you have side effects, your doctor may prescribe NINLARO capsules containing 3 mg or 2.3 mg. The doctor may also adjust the doses of the other medicines.

How and when to take NINLARO

- Take NINLARO at least one hour before or at least two hours after food.
- Swallow the capsule whole with water. Do not crush, chew or open the capsule.
- Do not let the contents of the capsule come into contact with your skin. If the powder accidentally comes into contact with your skin, wash it off thoroughly with soap and water. If the capsule breaks, clean up the powder, taking care that it does not cause dust in the air.

If you take more NINLARO than you should

If you take more NINLARO than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you.

Duration of the treatment with NINLARO

You should continue treatment until your doctor tells you to stop.

If you forget to take NINLARO

If a dose is missed or delayed, you should take the dose as long as the next scheduled dose is more than 3 days or 72 hours away. Do not take a missed dose if it is within 3 days or 72 hours of your next scheduled dose.

If you vomit after taking a dose, do not take an extra dose. Take the next dose, as normal, when it is due.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or pharmacist straight away if you notice any of these following very common serious side effects which may affect more than 1 in 10 people:

- low platelet counts (thrombocytopenia) which may increase the risk of nose bleeds and you may easily bruise
- nausea, vomiting and diarrhoea
- numbness, tingling or burning of the hands or feet (peripheral neuropathy)
- swelling of the legs or feet (peripheral oedema)
- skin rash that may be itchy and in a few areas or all over the body

Additionally, tell a doctor immediately if you notice any of these following rare side effects which may affect up to 1 in 1,000 people:

- severe skin rashes such as red to purple bumps (Sweet's syndrome) or rash with skin peeling and mouth sores (Stevens-Johnson syndrome)
- muscle weakness, loss of feelings of the toes and feet or loss of leg movement (transverse myelitis)
- changes in vision, changes in mental status, or seizures (posterior reversible encephalopathy syndrome)
- rapid death of cancer cells that may cause dizziness, decreased urination, confusion, vomiting, nausea, swelling, shortness of breath, or heart rhythm disturbances (tumour lysis syndrome)
- rare blood condition resulting from blood clots that may cause fatigue, fever, bruising, nose bleeds, decreased urination (thrombotic thrombocytopenic purpura)

Other possible side effects
Tell your doctor or pharmacist if any of the side effects below become severe.

Very common side effects may affect more than 1 in 10 people:

- constipation
- back pain
- cold-like symptoms (upper respiratory tract infection)
- feeling tired or weak (fatigue)
- lowered white blood cells called neutrophils (neutropenia) that may increase the risk of infection
- not feeling like eating (decreased appetite)
- irregular heart rate (arrhythmia)
- vision conditions including blurred vision, dry eye and pink eye (conjunctivitis)

Common side effects may affect up to 1 in 10 people:

- reactivation of the chicken pox virus (shingles) that can cause a skin rash and pain (herpes zoster)
- lowered blood pressure (hypotension)
- shortness of breath or persistent coughing or wheezing (heart failure)
- yellow discoloration of eyes and skin (jaundice which could be a symptom of liver impairment)
- low levels of potassium in the blood (hypokalaemia)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly to:

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie

E-mail: medsafety@hpra.ie

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store NINLARO

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister, wallet and carton after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C. Do not freeze.

Store in the original package in order to protect from moisture.

Do not remove the capsule until you need to take a dose.

Do not use this medicine if you notice any damage or signs of tampering to medicine packaging.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What NINLARO contains
NINLARO 2.3 mg hard capsule:
- The active substance is ixazomib. Each capsule contains 2.3 mg of ixazomib (as 3.3 mg of ixazomib citrate).
- The other ingredients are:
  - In the capsule: microcrystalline cellulose, magnesium stearate and talc.
  - The capsule shell contains: gelatin, titanium dioxide (E171) and red iron oxide (E172)
  - The printing ink contains: shellac, propylene glycol, potassium hydroxide, and black iron oxide (E172).

NINLARO 3 mg hard capsule:
- The active substance is ixazomib. Each capsule contains 3 mg of ixazomib (as 4.3 mg of ixazomib citrate).
- The other ingredients are:
  - In the capsule: microcrystalline cellulose, magnesium stearate and talc.
  - The capsule shell contains: gelatin, titanium dioxide (E171) and black iron oxide (E172)
  - The printing ink contains: shellac, propylene glycol, potassium hydroxide, and black iron oxide (E172).

NINLARO 4 mg hard capsule:
- The active substance is ixazomib. Each capsule contains 4 mg of ixazomib (as 5.7 mg of ixazomib citrate).
- The other ingredients are
  - In the capsule: microcrystalline cellulose, magnesium stearate and talc.

- The capsule shell contains: gelatin, titanium dioxide (E171), yellow iron oxide (E172) and red iron oxide (E172)
- The printing ink contains: shellac, propylene glycol, potassium hydroxide, and black iron oxide (E172).

What NINLARO looks like and contents of the pack
NINLARO 2.3 mg hard capsule: Light pink, size 4, marked “Takeda” on the cap and “2.3 mg” on the body with black ink.

NINLARO 3 mg hard capsule: Light grey, size 4, marked “Takeda” on the cap and “3 mg” on the body with black ink.

NINLARO 4 mg hard capsule: Light orange, size 3, marked “Takeda” on the cap and “4 mg” on the body with black ink.

Each pack contains 3 hard capsules (three single cartons, each containing a blister sealed inside a wallet. Each blister contains one capsule).

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.