

Ixazomib (Ninlaro®)

What is ixazomib?

Like bortezomib (Velcade®) and carfilzomib (Kyprolis®), ixazomib belongs to a group of drugs known as proteasome inhibitors.

Ixazomib is the first oral (by mouth) proteasome inhibitor to be developed, this means it can be taken at home as a tablet instead of being administered in the hospital.

How does ixazomib work?

Proteasomes are large molecules which are present in all cells in the body. They are involved in the removal, breakdown and recycling of damaged proteins or those that are no longer needed by the cell. Proteasome inhibitors work by binding to proteasomes and temporarily blocking their function, which stops them from breaking down unwanted proteins. This causes proteins to build up and become toxic, killing the cell.

Myeloma cells multiply more quickly than normal healthy cells and rely more heavily on proteasomes as they produce unwanted proteins at a faster rate. Myeloma cells are therefore much more sensitive to ixazomib than normal cells.

Myeloma cells appear to be even more dependent on the actions of proteasomes than other types of cancer cells. This may be due to the need of the myeloma cells to dispose of the abnormal protein (paraprotein) they produce.

By blocking the function of the proteasome, ixazomib prevents the myeloma cells from growing and multiplying.

How is ixazomib given?

Ixazomib can be given on its own or in combination with other myeloma treatments. It is usually taken on days 1, 8 and 15 of a 28 day cycle.

Ixazomib is usually continued until the myeloma is showing signs of increasing.

When is ixazomib available for use in Australia on the Pharmaceutical Benefits Scheme (PBS)?

The Australian Therapeutic Goods Administration (TGA) have approved ixazomib as a safe and effective treatment. However, it has not yet been listed to be subsidised by the Pharmaceutical Benefits Scheme (PBS).

It may be available via clinical trials in some states. Ask the doctor if a clinical trial is an appropriate option when new treatment is required.

How to tell if ixazomib is working?

Patients may observe a reduction in the symptoms caused by the myeloma associated with an improved quality of life. The doctor will also order tests at the start of each treatment cycle to monitor response. These tests may vary from patient to patient but generally include regular blood and/or urine testing and occasional x-rays or bone marrow biopsies.



What are the potential side effects?

Low blood counts

Ixazomib can cause a decrease in the number of white blood cells and platelets in the blood.

A low white blood cell count will increase the risk of infection. People taking ixazomib are more susceptible to shingles infections. To avoid infections, extra precautions will be required such as diligent hand washing and avoidance of people with infections. A sign of infection is a fever or temperature of 38°C or above.

If a patient's temperature is 38°C or above, medical attention must be sought immediately

If the white cell count is consistently low, it may be necessary to have an injection of granulocyte-colony stimulating factor (G-CSF), to increase the white blood cell count. The doctor will also prescribe medication to help prevent infections.

A low platelet count (thrombocytopenia) increases the risk of bruising and bleeding. If the platelet count is too low a platelet transfusion may be required.

The blood counts will be measured regularly to monitor for changes. In some cases, treatment may be delayed until blood counts have improved.

Fluid retention/swelling

Some people taking ixazomib will experience fluid retention or swelling in the arms, hands, feet or ankles or may notice an increase in their overall weight. Notify the doctor if this happens so they can address the issue.

Diarrhoea

Whilst usually mild and easily manageable, diarrhoea can become problematic in some cases but easily managed with simple treatments. It is important to alert the doctor as soon as symptoms commence as there is a risk of dehydration when experiencing diarrhoea.

Constipation

A decrease in the normal frequency of bowel movements may occur whilst taking ixazomib. It may be accompanied by gas, pain, or pressure in the stomach. Constipation is usually easier to prevent than to treat.

To relieve the symptoms of constipation, patients can eat a healthy diet which is high in fibre. Fibre absorbs water making stools softer, bulkier and easier to eliminate. Drinking plenty of fluids (aim for about 8 glasses of water a day) helps the fibre work. Pear or prune juice may also help. Regular gentle exercise keeps the bowels more active to help move things along. Gentle laxatives (consult a nurse or pharmacist) may be needed but if constipation continues to be a problem, talk with the doctor.

Nausea and vomiting

Less than a quarter of people having ixazomib therapy will experience nausea and vomiting. Anti nausea medication can be prescribed to prevent and treat these symptoms.

Peripheral neuropathy

While ixazomib is far less likely to cause peripheral neuropathy than its cousin bortezomib, it can in some cases cause damage to the long nerves radiating from the spine, usually starting in the hands and/or feet then progressing up the arms and legs. This can present as feelings of numbness, tingling, increased sensitivity, burning, pain or cramps. It can also present as constipation, dizziness, or loss of balance.

The best way to manage peripheral neuropathy is to report any symptoms to the doctor or nurse as soon as possible. They may recommend a dose reduction or taking a break until symptoms subside. The effects of peripheral neuropathy can be irreversible if left unattended for too long.

For more information about peripheral neuropathy and cramps, please see the *Managing Peripheral Neuropathy Book – A guide for people with myeloma* at www.myeloma.org.au or call head office for a copy.

Skin rashes

Ixazomib can sometimes cause a rash which may begin on the trunk (body) and spread to the arms and legs. This can occur within the first few weeks of starting treatment but usually clears up by itself. Sometimes the rash may need treatment. If the rash continues and is problematic, the dose of ixazomib may be reduced or stopped temporarily. Rarely, rashes may be a more serious side effect of ixazomib where skin can turn red, blister and peel (Stevens Johnson syndrome or toxic epidermal necrolysis). If this happens, you should inform your doctor immediately and ixazomib should be stopped straightaway.

Back pain

Many people experience back pain as part of their myeloma. If this pain changes, or you notice a new pain in the back, notify the doctor who will investigate the cause.

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For further information please contact our Myeloma Support Nurses on our toll free Support Line:

1800 MYELOMA (1800 693 566)
or visit our website: **www.myeloma.org.au**