

Bortezomib (Velcade®)

What is bortezomib?

Bortezomib (Velcade®) belongs to a group of drugs known as proteasome inhibitors. It is in the same family as carfilzomib (Kyprolis®) and ixazomib (Ninlaro®).

How does bortezomib 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 bortezomib 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, bortezomib prevents the myeloma cells from growing and multiplying.

How is bortezomib given?

Bortezomib is given as an injection under the skin (subcutaneous), or in some cases it can be given as an injection into the vein (intravenous). It has been shown to be most effective when used in combination with other myeloma treatments such as chemotherapy and steroids.

Bortezomib is often given on days 1, 8, 15 and 22 or a 28 or 35 day cycle. In some cases it may be given on days 1, 4, 8 and 11 of a 28 day cycle.

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

Bortezomib is subsidised on the PBS for people who are newly diagnosed or if another treatment was prescribed at diagnosis, it can be given at a later date. The number of cycles subsidised depends on whether there is a plan for an autologous stem cell transplant and if the bortezomib is proving effective after a certain amount of time.

If bortezomib has been effective during one stage of the disease, the PBS will subsidise treatment again at relapse.

How to tell if bortezomib 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 possible side effects?

Peripheral neuropathy

Bortezomib can 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 and pain. 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.

Cramps

A cramp is an uncontrollable and painful spasm of a muscle and may also be accompanied by twitching. Twitching is an involuntary contraction then relaxation of a muscle which is sometimes caused by nerve damage from bortezomib. Cramps and twitches often occur at night as muscles try to relax. Gentle stretching, massage and ensuring adequate salt balance in the body can help relieve the symptoms of cramps.

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.

Low blood counts

Bortezomib can cause a decrease in the number of red blood cells, white blood cells and platelets in the blood. A low red blood cell count may cause anaemia and fatigue. If anaemic a blood transfusion may be necessary.

A low white blood cell count will increase the risk of infection and 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.

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 bortezomib. 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

Some people on bortezomib therapy will experience nausea and vomiting. Anti nausea medication can be prescribed to prevent and treat these symptoms.

Fatigue

Many patients on bortezomib experience fatigue. It can be difficult to distinguish between fatigue that is directly related to bortezomib treatment and fatigue that is caused by the myeloma itself. A balanced diet, adequate fluid intake, regular exercise and adequate sleep can help minimise the effects of fatigue.

Precautions

It is recommended to avoid drinking copious amounts of green tea and consuming high amounts of vitamin C while on bortezomib treatment as they reduce the efficacy of the therapy.

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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**