



## About us

The Leukaemia Foundation is Australia's peak body for blood cancer, funding research and providing free services to support people with leukaemia, lymphoma, myeloma and related blood disorders.

We invest millions of dollars in the work of Australia's leading researchers to develop better treatments and cures and provide free services to support patients and their families.

We receive no ongoing government funding. We rely on the generosity of the community and corporate sector to further our Vision to Cure and Mission to Care.

## We can help you

Our range of free services supports thousands of Australians, from diagnosis, through treatment and beyond. To learn more, please call 1800 620 420 to speak with one of our Support Services team.

## You can help us

There are many ways that you can help us to improve the quality of life for people with blood cancer. From making a donation, to signing up for an event, from volunteering, or joining us as a corporate sponsor - please call 1800 500 088 or go to [www.leukaemia.org.au](http://www.leukaemia.org.au) to learn more.

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## What is Bortezomib?

**Bortezomib is the first in a new class of anti-cancer drugs called proteasome inhibitors. Proteasomes are a group of enzymes found in all cells in the body. They play an important role in controlling cell function and growth.**

In Australia the cost of bortezomib is subsidized by the government under the Pharmaceutical Benefits Scheme (PBS) for the treatment of newly diagnosed myeloma patients who have not had any prior treatment for their myeloma (also referred to as "upfront or frontline therapy"). Bortezomib is also approved for patients who have received one or more prior treatments and the myeloma is still progressing. Since its introduction, bortezomib has had a significant impact on the treatment of myeloma. It is highly effective in targeting myeloma cells resulting in a rapid reduction in paraprotein levels in many patients.

Data from trials in newly diagnosed myeloma patients show that bortezomib used in combination with other therapies is superior in achieving high rates of response compared to combinations of other therapies (such as melphalan and prednisolone) without bortezomib. Bortezomib continues to be studied in combination with other marketed anti-myeloma medications and in combination with medications in development.

### How does bortezomib work?

Bortezomib works by temporarily blocking the action of proteasomes. Proteasomes are enzymes found in cells which are involved in the removal, breakdown and recycling of damaged or unwanted proteins. As a consequence of temporarily blocking the actions of proteasomes, these damaged or unwanted proteins build up and become toxic, causing the cell to die. Myeloma cells rely more heavily on proteasomes than normal healthy cells and are therefore much more sensitive to bortezomib.

Through its action of blocking the functioning of the proteasome, bortezomib is thought to work in the following ways:

- Directly killing myeloma cells
- Altering the production of chemical signals crucial for the growth and survival of myeloma cells
- Preventing myeloma cells from sticking to bone marrow stroma (supportive cells)
- Blocking the growth of new blood vessels (anti-angiogenesis) that supply myeloma cells with oxygen and nutrients

### How is bortezomib administered?

Bortezomib is given by a quick injection intravenously (into the vein) or subcutaneously (under the skin). When given by intravenous injection bortezomib is given over three to five seconds. When given by subcutaneous injection bortezomib may be better tolerated (with fewer severe side effects) and may be less likely to cause significant peripheral neuropathy than intravenous injection. Given twice weekly, subcutaneously bortezomib is considered as effective as intravenous injection.

When given on its own, bortezomib is usually given as four doses over a three-week period. The doses are given on days 1, 4, 8 and 11, followed by a 10 day rest period. This completes one cycle of treatment. There can be up to eight cycles of treatment over six months. Bortezomib may also be given as a weekly injection. Some studies have shown it is just as effective as twice-weekly dosing but may have fewer side effects, including a significantly reduced risk of peripheral neuropathy. The number of treatment cycles will depend upon what has been approved by the PBS for your particular stage in your myeloma treatment.

As treatment for myeloma is often more effective when two or more drugs are given together, bortezomib is usually given with other drugs effective in the treatment of myeloma. Most commonly bortezomib is given with the corticosteroid dexamethasone. Other anti-myeloma medications such as chemotherapy agents (eg cyclophosphamide, melphalan or doxorubicin) may also be used in combination.

Your treating doctor will discuss with you the most suitable way to give your bortezomib depending on what options are available at your hospital and the one which may be best used in your individual case. This can depend on such factors as, the nature of your myeloma, side effects you have experienced and the likelihood of being able to tolerate bortezomib.

### **What are the side effects of bortezomib?**

As with all medications, bortezomib has a number of potential side-effects. They vary considerably from person to person and may be mild or more serious. As side-effects can usually be managed, it is very important to discuss any side-effects you are experiencing with your health care professional.

Before the dose of bortezomib is given a health professional will ask you questions about any side-effects you may be experiencing. The health professional will offer advice on the best way to manage side-effects. You may also need blood tests taken and the results reviewed, before the dose of bortezomib is given. Sometimes because of side-effects or blood results the dose of bortezomib may need to be decreased or withheld.

The most common side-effects of bortezomib include:

- **Peripheral neuropathy**

Peripheral neuropathy is the term used to describe damage to the nerves in the hands, feet, arms or legs. Peripheral neuropathy can cause numbness, tingling, increased sensitivity and pain. Some people may notice that they have difficulty buttoning clothes or doing fiddly tasks or they may experience painful, restless legs. It is important to be aware that peripheral neuropathy in myeloma can also be caused by the actual protein deposits from myeloma (10 – 20%) and also from other forms of treatment that may be used such as thalidomide and vincristine. Peripheral neuropathy can affect up to 50% of people treated with bortezomib. The best way to prevent worsening peripheral neuropathy is to discuss any symptoms such as numbness, tingling and any changes in sensation to your hands and feet with your health care professional as soon as possible. It is important that monitoring for peripheral neuropathy occurs frequently. If it is detected early and the dose of bortezomib reduced early this side effect is manageable. If symptoms are more severe, bortezomib may be stopped for a time until the symptoms improve and then restarted at a lower dose. Studies have shown that the severity of the peripheral neuropathy may be reduced by giving bortezomib subcutaneously or weekly.

Another type of neuropathy that can be caused by bortezomib is called autonomic neuropathy. This can be experienced as dizziness on standing. Some people taking bortezomib feel dizzy or light-headed if they stand up quickly. This is caused by a temporary drop in blood pressure. Drinking plenty of fluids and moving slowly when getting up from a lying or sitting position can help. Care should also be taken when driving a vehicle or operating machinery. Some people who are on blood pressure lowering medication may need to have their blood pressure treatment reduced or stopped whilst they are on bortezomib.

- **Tiredness (fatigue)**

Feeling tired is a common side effect of bortezomib. It's important to pace yourself and get as much rest as needed. Gentle exercise, such as short walks, can also help. Care should be taken as tiredness may affect your ability to drive or operate machinery. Tiredness caused by bortezomib usually improves after the treatment has finished.

- **Feeling sick (nausea) and being sick (vomiting)**

It is important to report nausea or vomiting. You will receive medication to prevent the nausea and vomiting, however if these medications are not fully effective please notify your healthcare professional so you may be given additional medications.

- **Loss of appetite and taste changes**  
Some people lose their appetite while they're being treated with bortezomib. This can be mild and may only last a few days. If your appetite doesn't improve a dietitian or specialist nurse can provide advice on maintaining a healthy diet. Sometimes the taste of food and drinks can also be affected by bortezomib. A dietitian or specialist nurse can also give advice on ways of managing this side-effect.
- **Constipation or diarrhoea**  
Bortezomib can cause constipation or diarrhoea. Constipation can usually be helped by drinking plenty of fluids, eating more fibre and doing some gentle exercise. If constipation is severe or continues for more than three days, please discuss with your health care professional as laxatives may be required. Diarrhoea can usually be easily controlled with medication, however please inform your health care professional if the diarrhoea is severe or continues for longer than 2-3 days. It's important to drink plenty of fluids if you have diarrhoea.
- **Risk of infection**  
Bortezomib can sometimes reduce the number of white blood cells. White blood cells are produced by the bone marrow and they help to fight infections. If the number of white blood cells is low, then you may be at increased risk of infection. It is important to monitor your temperature when your white cell count is low. There are also other special precautions, such as avoiding crowded places and asking family and friends if they have an infection (such as a cold or cough) not to visit. If the white cell count is very low medication may be given by injection to increase the white cell count e.g. filgrastim, pegfilgrastim. Bortezomib can lower your immune system which increases the risk of you developing shingles (herpes zoster virus). Anti-viral drugs are usually given to help reduce the risk of shingles.
- **Bruising and bleeding**  
Bortezomib can reduce the production of platelets by the bone marrow. Platelets help the blood to clot and hence stop bleeding. It is important to report any unexplained bruising or bleeding, such as nosebleeds, bleeding gums, blood spots or rashes on the skin. A platelet transfusion may be given if the platelet count is very low.
- **Anaemia (low number of red blood cells)**  
Bortezomib can reduce the number of red blood cells produced by the bone marrow. Red cells carry oxygen around the body. A low red blood cell count is called anaemia. Anaemia causes tiredness and breathlessness. A blood transfusion may be given if the number of red blood cells becomes too low. The blood counts are monitored each time a person goes for bortezomib treatment to check that they are within the normal range. In some cases, the next treatment with bortezomib may be delayed until the blood counts have improved. This may take a few weeks but should not affect the activity of the myeloma and it does not mean the myeloma will suddenly progress without immediate treatment.
- **Skin rashes**  
Some myeloma patients on bortezomib may develop an itchy skin rash which can be treated with antihistamines and/or corticosteroid creams. If this is particularly troublesome, bortezomib may need to be stopped temporarily and restarted at a lower dose.

### **Other medicines may interact with bortezomib**

Some medicines, including those that you can buy in a shop or pharmacy, can interact with bortezomib and potentially affect its action on the myeloma cell. This means it may reduce the action of bortezomib and therefore make it less effective as a treatment for you. It is important that your health care professional is aware of any other medications you are taking, including over-the-counter drugs, complementary therapies and herbal drugs. Examples are high dose Vitamin C and green tea supplements where these drugs have been shown to block bortezomib activity in the laboratory and therefore high dose supplements should be avoided whilst on treatment.

It is important to mention any symptoms, even if they seem trivial to your treating doctor. The treating doctor can then adjust your treatment accordingly.

It is not the intention of this fact sheet to recommend any particular form of treatment to you. You need to discuss your particular circumstances at all times with your treating doctor. For more information, Freecall 1800 620 420, email [info@leukaemia.org.au](mailto:info@leukaemia.org.au) or visit [www.leukaemia.org.au](http://www.leukaemia.org.au)