

Carfilzomib (Kyprolis®)

What is carfilzomib?

Carfilzomib belongs to a group of drugs known as proteasome inhibitors which is the same family of drugs as bortezomib (Velcade®) and ixazomib (Ninlaro®). Carfilzomib has been developed to target a different part of the proteasome to bortezomib. This is thought to make carfilzomib more effective and potentially cause fewer side effects than bortezomib.

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

How is carfilzomib given?

Carfilzomib is given as an up to 30 minute intravenous (IV), into the vein infusion. The dose will be calculated on the patient's height and weight and will begin as a smaller dose for the first cycle. Then if there are no major side effects of concerns, the dose will be increased. For the first cycle only, IV hydration will be given prior to the carfilzomib infusion.

Carfilzomib will be given on days 1, 2, 8, 9, 15 and 16 of a 28 day cycle.

Carfilzomib is often given in combination with other medications to increase the efficacy. It is continued until the myeloma shows signs it is beginning to become active again or if the side effects of treatment become intolerable.

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

Carfilzomib is subsidised through the PBS in combination with a steroid medication, dexamethasone for patients whose myeloma has returned after already having one type of treatment.

It is also possible to have carfilzomib as part of a clinical trial in combination with other therapies. The doctor can advise when a clinical trial is appropriate.

How to tell if carfilzomib 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?

As with all drugs, carfilzomib has many potential side effects. They can vary considerably from patient to patient and may be mild or more serious. Often the best way to reduce side effects is to lower the dose. It is possible to do this without compromising on efficacy. As side effects can usually be treated or managed, it is very important to highlight them promptly to the doctor or nurse.

Heart problems

Carfilzomib has been found to cause heart problems or worsen pre existing heart conditions. Therefore, patients being treated with carfilzomib will be monitored carefully during treatment. Symptoms of heart problems include high blood pressure, shortness of breath, chest pain and swelling in the lower limbs and/or hands.

It is important to tell the doctor about any history of heart problems before starting carfilzomib and to report any of the above side effects immediately once treatment starts.



Lung problems

Some people will experience lung problems while on carfilzomib therapy. Symptoms of lung problems include difficulty breathing, shortness of breath and cough. It is important to report these symptoms to the doctor immediately

Low blood counts

Carfilzomib 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. People having carfilzomib treatment are especially susceptible to upper respiratory tract and 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.

Blood clots or venous thromboembolic events

Developing a blood clot in deep veins is a potentially serious side effect of treatment with carfilzomib. The condition is called deep vein thrombosis (DVT). Symptoms include redness, swelling, tenderness and pain. If patients develop any of these symptoms, the doctor must be informed immediately. Sometimes a piece of the clot breaks off and travels to the lung. This can be life threatening and is called pulmonary embolism (PE). Symptoms of PE include anxiety, shortness of breath with or without exertion and chest pain/tightness. Patients must seek medical assistance urgently if these symptoms occur.

Each person is assessed for their risk of VTE and may be prescribed an anticoagulant drug such as aspirin or low-dose heparin to prevent (prophylaxis) or to treat VTE.

Fatigue

Many patients on carfilzomib experience fatigue. It can be difficult to distinguish between fatigue that is directly related to carfilzomib 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.

Nausea and vomiting

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

Peripheral neuropathy

While carfilzomib 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.

Fever

A fever is a temperature of 38°C or above. In people who are having carfilzomib therapy it may be a sign of infection or an infusion reaction. A steroid medication, dexamethasone is given at least 30 minutes before the infusion to prevent infusion reactions.

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

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 carfilzomib. 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.

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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**