# Carfilzomib (Kyprolis®)

**This Horizons Infosheet contains information on carfilzomib (also known as Kyprolis®), a drug being investigated for the treatment of myeloma.**

The Horizons Infosheet series provides information relating to novel drugs and treatment strategies that are currently being investigated for the treatment of myeloma. The series also aims to highlight the considerable amount of research currently taking place in the field of myeloma.

The drugs and treatment strategies described in the Horizons Infosheets may not be licensed and/or approved for use in myeloma. You may, however, be able to access them as part of a clinical trial.

## What is carfilzomib?

Carfilzomib is a new drug being used to treat myeloma.

Like bortezomib (Velcade®), carfilzomib belongs to a group of drugs known as proteasome

inhibitors. Carfilzomib works in a similar way to bortezomib however it has been developed to target a different part of the proteasome. This is thought to make carfilzomib more effective and potentially cause fewer side-effects than bortezomib.

## What are proteasomes?

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.

## How does carfilzomib work?

Carfilzomib works by binding to proteasomes and permanently blocking their function which stops them from breaking down unwanted proteins (Figure 1). 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.

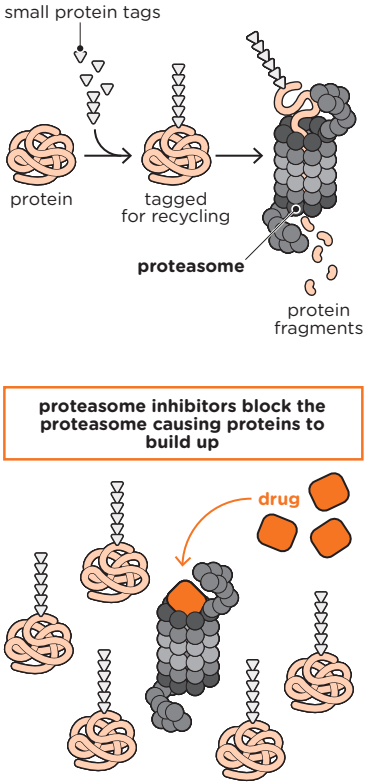


**Figure 1. Mechanism of action of proteasome inhibitors**

## How is carfilzomib given?

Carfilzomib is given as an intravenous (into the vein) infusion. It has been shown to be most effective when used in combination with other myeloma treatments such as lenalidomide (Revlimid®) and dexamethasone.

### Carfilzomib and dexamethasone

When given in combination with dexamethasone only, carfilzomib is administered over a 28-day treatment cycle. It is administered as a 30-minute infusion starting at 20mg/m$^2$ (your height and weight will be measured to find the correct dose) over 2 consecutive days each week for 3 weeks. If this dose is tolerated it is increased to 56mg/m$^2$ for the remaining cycles.

Low-dose dexamethasone (20mg/m$^2$) is given on days 1, 2, 8, 9, 15 and 16 of a cycle.

Carfilzomib with dexamethasone is given until the myeloma shows signs it is beginning to become active again.

### Carfilzomib, lenalidomide and dexamethasone

When given in combination with lenalidomide and dexamethasone, carfilzomib is administered over a 28-day treatment cycle. Carfilzomib is given over 2 consecutive days each week for 3 weeks followed by 12 days off. It is administered as a 10-minute infusion starting at 20mg/m$^2$ on days 1 and 2 of the first cycle. If this dose is tolerated, the dose is increased to 27mg/m$^2$ for the remaining cycles.

Patients receive lenalidomide each day on days 1 to 21 and dexamethasone on days 1, 8, 15 and 22 of each cycle.

Carfilzomib is given for a maximum of 18 cycles when given with lenalidomide and dexamethasone.

## What evidence exists to support the use of carfilzomib?

In the Phase III ASPIRE clinical trial, progression free survival (the length of time following tretment before the myeloma returns) increased from an average of 17.6 months in those being treated with lenalidomide and dexamethsone to 26.3 months in those being treated with carfilzomib, lenlidomide and dexamethasone.

Further evidence from the Phase III ENDEAVOR clinical trial found that progression free survival nearly doubled (17.6 months compared to 9.4 months) in

patients treated with carfilzomib and dexamethasone compared to patients who had bortezomib and dexamethasone.

Carfilzomib is currently being investigated in combination with other myeloma treatments. For example, the MUK five trial is investigating the use of carfilzomib with cyclophosphamide and dexamethasone. Initial results from this trial have found an overall response of nearly 88% (14 of 16 patients treated).

In ongoing trials, carfilzomib is proving to be an effective initial treatment for newly diagnosed myeloma patients.

Research into carfilzomib as a monotherapy (on its own and not in combination with other drugs) has found that it is not as effective as when it is given in combination with other drugs.

## What are the known possible side-effects of carfilzomib?

The most commonly reported side-effects of carfilzomib include: fatigue, low platelet counts (thrombocytopenia), low red blood cell counts (anaemia), nausea, difficulty breathing, diarrhoea and fever.

Carfilzomib has also been found to cause heart problems or worsen pre-existing heart conditions. Therefore, patients being treated with carfilzomib will be monitored carefully during treatment.

Though carfilzomib is from the same drug family as bortezomib, it is thought to cause much lower rates of peripheral neuropathy (damage to the nerves that make up the peripheral nervous system causing pain, tingling and altered sensation).

## Is carfilzomib currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving carfilzomib, visit the **Myeloma Trial Finder** on **www.myeloma.org.uk**

To be enrolled on a clinical trial, patients have to meet certain conditions known as eligibility criteria. You should speak to your doctor in the first instance if you are interested in taking part in a trial.

## UK availability of carfilzomib

Before a drug can be widely used, it must first be licensed as a safe and effective treatment. This is usually done by regulatory authorities at a European level

and involves a review of evidence from large-scale clinical trials. Normally, the licensed drug must then be approved by a UK drug appraisal body before it can be routinely prescribed by NHS doctors. The drug appraisal process differs from licensing – it compares how effective the newly-licensed drug is to existing drugs already in use on the NHS and decides whether it offers the NHS good value for money. The main body responsible for carrying out drug appraisals in England and Wales is the National Institute for Health and Care Excellence (NICE). NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal body is the Scottish Medicines Consortium (SMC).

**For more information see the Health Technology Assessment (HTA) Infosheet from Myeloma UK**

Carfilzomib has been approved by the European licensing body, the European Medicines Agency (EMA) for relapsed myeloma patients who have received at least one previous treatment.

In June 2017, carfilzomib was approved for use in England and Wales in combination with dexamethasone for myeloma patients at first relapse, who have had one previous treatment that did not include bortezomib. The approval was dependent on the inclusion of a patient access scheme – a way of giving a discount on the price of a drug to improve its cost-effectiveness.

NICE has not recommended carfilzomib for use in combination with lenalidomide and dexamethasone in relapsed myeloma patients. NICE issued negative guidance for this triplet combination because of its uncertainty about whether it represented a cost-effective use of NHS resources.

In Scotland, the SMC has also turned down carfilzomib in combination with lenalidomide and dexamethasone for relapsed myeloma patients. This is because it felt the submission did not justify the cost of the treatment to the NHS. However, in August 2017 the SMC approved carfilzomib in combination with dexamethasone alone in relapsed myeloma patients.

## Future directions

Carfilzomib continues to be studied in different patient groups and in different treatment

combinations. These trials will provide information about the safest and most effective way to use carfilzomib in myeloma.

## About this Horizons Infosheet

The information in this Horizons Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

For a list of references used to develop our resources, visit **www.myeloma.org.uk/references**

To provide feedback about this publication, email **myelomauk@myeloma.org.uk**

## Other information available from Myeloma UK

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma UK Infoline on **0800 980 3332** or **1800 937 773** from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at **www.myeloma.org.uk**


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