

Myeloma Infoguide Series



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Introduction

This Infoguide is written for patients with myeloma and their families and friends. It provides information on VELCADE® (bortezomib), a new type of myeloma treatment

This Infoguide reviews what Velcade is, how it works, when it is used in myeloma, what to expect from treatment and what potential side-effects may occur.

Some of the more technical or unusual words appear in bold the first time they are used and are explained in the **Medical terms explained** section at the back of the Infoguide

Aims of this Infoguide

- To provide you with more information on Velcade treatment
- To answer some of the more common questions around Velcade
- To help you make informed decisions about the treatment options available

Myeloma UK provides a range of specific Infoguides and Infosheets which cover all aspects of the treatment and management of myeloma. You will find a list of these at the back of this Infoguide.

If you would like a more general overview of what myeloma is, how it is diagnosed, the most commonly used treatments and many of the things you may have to cope with in living with myeloma, please see *Myeloma - Your Essential Guide* and *Living with Myeloma - Your Essential Guide*. To order your free copies contact the **Myeloma Infoline on 0800 980 3332**. This information is also available 24/7 on our website at www.myeloma.org.uk

If you would like to talk to someone about any aspect of myeloma, its treatment and management, call the **Myeloma Infoline on 0800 980 3332**. Your call will be answered by Myeloma Information Nurse Specialists who are supported by medical and scientific advisors. The Myeloma Infoline is open Monday to Friday, 9am to 5pm, and is free to phone from anywhere in the UK. From outside the UK, call +44 131 557 3332 (charged at normal rate).

Disclaimer

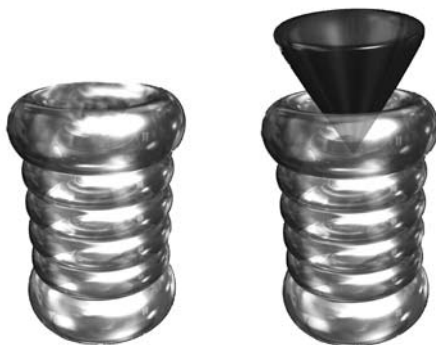
The information in this Infoguide is not meant to replace the advice of your medical team. They are the best people to ask if you have questions about your individual situation.

What is Velcade and how does it work?

Velcade is the first in a new class of anti-cancer drugs called proteasome inhibitors and is the first drug to be approved for the treatment of myeloma in over 10 years.

Proteasome inhibitors have a unique mechanism of action and work differently from standard **chemotherapy**. This is very important as they can therefore be used alongside chemotherapy or instead of it when it stops working.

Proteasome with proteins enter at the top and waste proteins (peptides) leave at the bottom



Velcade acts like a cone to block the proteasome causing protein build-up

Figure 1 – Proteasomes

The proteasome, which is found in all cells, works by breaking down the many different proteins that control the life-cycle of cells. Velcade works by temporarily blocking the function of the proteasome, resulting in a build-up of proteins which confuses the cell and causes it to die.

However, unlike the healthy cells which can recover within less than 72 hours, myeloma cells are between 100–1000 times more sensitive to Velcade and therefore cannot recover. The quick recovery of normal healthy cells can also prevent certain **side-effects** such as hair-loss occurring.

How does Velcade affect myeloma?

By blocking the proteasome, Velcade can affect the growth and survival of myeloma cells through multiple mechanisms of action.

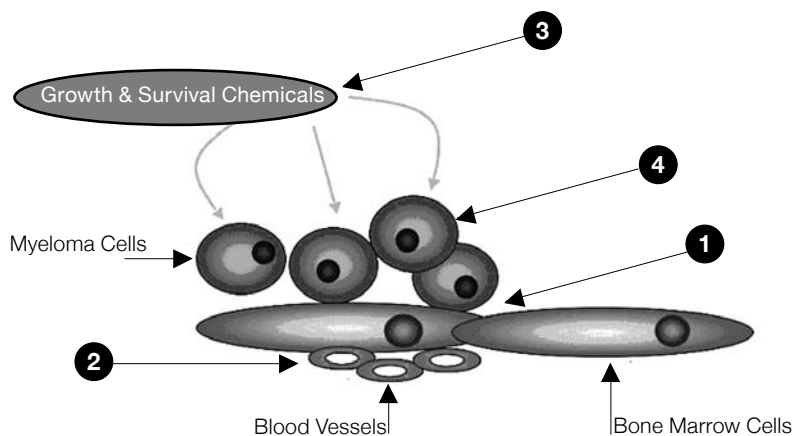


Figure 2 - The different ways Velcade can affect myeloma

These include:

- 1 Preventing the myeloma cells from sticking to bone marrow cells
- 2 Inhibiting the growth of new blood vessels which supply the myeloma cells with oxygen and nutrition
- 3 Altering the production of chemicals crucial for the growth and survival of myeloma cells
- 4 Velcade may also have a direct killing effect on the myeloma cells

How is Velcade used in myeloma?

The introduction of Velcade as a treatment for myeloma has been arguably one of the most important treatment breakthroughs in the last 40-50 years.

When it was first made available in 2004 outside of **clinical studies**, it was used in patients who had relapsing or refractory disease and who had received at least two previous treatments.

More recently, its use was extended to include patients whose myeloma had relapsed or had become refractory after having had just one prior treatment.

Its use in both these groups of patients was as monotherapy, i.e. on its own. However, it is almost always now used in combination with the steroid dexamethasone as it has been shown that when Velcade and dexamethasone are given together they produce a greater effect than when each is given on its own.

Clinical studies are now also underway to investigate how best to use Velcade, its role at other stages of the disease and in combination with both other standard and new treatments.

What follows, is a brief summary of the use and activity of Velcade at the various different stages of myeloma.

For more information about clinical studies, please see Myeloma UK's Infoguides *Clinical Studies* and *MRC Myeloma IX*. To order your free copies, contact the Myeloma Infoline on 0800 980 3332.

Relapsed or refractory disease as monotherapy

As already mentioned, Velcade has been shown to be effective in patients who have relapsed or refractory disease after having received at least two prior treatments.

The pivotal study in this group of patients showed an overall response rate to Velcade of 43% lasting on average for one year.

This study also showed an extended survival benefit when compared to the group of patients who received dexamethasone alone.

Combination with dexamethasone

Velcade may be given with the steroid dexamethasone either at the start of treatment, or if there is no response to Velcade alone after the first two or three cycles.

In patients who don't respond to Velcade alone, adding dexamethasone has produced a response in a further 20% of patients. The improved response included patients who had previously not responded to dexamethasone alone.

The combined, improved effectiveness of Velcade and dexamethasone means that current standard practice is usually to prescribe both together from the start.

Patients who have received just one prior treatment

Studies comparing Velcade with high-dose dexamethasone in patients who have received at least one prior treatment have shown Velcade to be more effective.

In patients receiving Velcade:

- More than 40% of patients responded
- Responses were not as good when it was used later in the disease
- A higher number of patients achieved a complete response
- Responses lasted longer
- Overall survival was better

These results therefore suggest a benefit from using Velcade as early in the disease as possible.

Newly-diagnosed patients and combination therapy

The positive results from these trials have prompted new studies investigating the role of Velcade in patients with newly-diagnosed myeloma, particularly in combination with other treatments.

Combinations under investigation include Velcade with dexamethasone and thalidomide (VTD), Velcade with adriamycin and dexamethasone (PAD), and Velcade with melphalan and prednisolone (VMP).

Although results from these studies look promising, it is early days and doctors are still not sure on the best and safest way to use Velcade in newly-diagnosed patients.

It is recommended therefore that Velcade should only be given to newly-diagnosed patients as part of a clinical study.

For more information on the treatment of myeloma, please see Myeloma UK's booklet *Myeloma– Your Essential Guide*. Myeloma UK also has a range of Infoguides on specific treatments, such as thalidomide. To order your free copies of these booklets, contact the **Myeloma Infoline on 0800 980 3332**.

How is Velcade given?

Velcade is given as a quick injection into a vein (intravenously) lasting only three to five seconds.

Before each dose of Velcade, blood tests may be taken and the results of these examined before the injection can be given. Hydration with intravenous fluids may also be given before Velcade is administered as this helps to protect and flush the vein. This means that it may take up to half a day to receive the Velcade treatment.

Velcade is given in a 21-day cycle. It is injected twice weekly for two weeks (days 1, 4, 8 and 11) followed by a 10-day rest period (days 12 to 21).

Usually this means it is given on a Monday and Thursday or on a Tuesday and Friday.

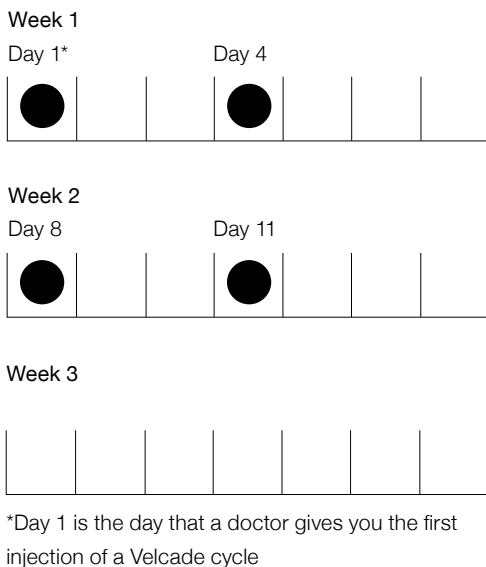


Figure 3 - One Velcade cycle

What is the best dose?

The starting dose for Velcade is normally 1.3 mg/m². Height and weight are used to calculate the exact dose for each patient.

The dose may be reduced or the drug withdrawn temporarily during treatment if certain side-effects are experienced. There is evidence that, where necessary, using a lower dose of Velcade is still effective in treating myeloma, whilst producing less side-effects.

Is Velcade best given alone or in combination?

There is evidence that better outcomes can be achieved when Velcade is given in combination with other myeloma treatments such as dexamethasone. The decision to give Velcade on its own or as part of a combination will be based on the individual disease and clinical factors together with doctor and patient preference.

For how long is Velcade given?

The ideal length of Velcade treatment has not been established and will vary from patient to patient and in which combination it is given.

Currently Velcade can be given for up to eight cycles. If there is no response within two or three cycles (when given with dexamethasone), Velcade treatment would normally be stopped and other options discussed.

The best way to use Velcade is still under investigation in myeloma clinical studies.

What are the potential side-effects of Velcade?

In general, the side-effects of Velcade are mild to moderate, however this can vary considerably from patient to patient. It is important to highlight side-effects promptly to nurses and doctors as they can usually be easily treated or managed.

Often the best way to reduce side-effects is to lower the dose of Velcade.

There is evidence that a lower dose of Velcade is still effective but produces fewer side-effects. Unfortunately, if side-effects remain troublesome, it may be necessary to stop treatment altogether and consider other options.

The most common side-effects include gastrointestinal effects (diarrhoea, nausea, vomiting, constipation), reduced levels of blood cells, fatigue, and a nerve disorder called peripheral neuropathy. These are explained in more detail below.

Gastrointestinal

Velcade has been shown to cause diarrhoea, constipation, nausea and vomiting. Whilst usually mild to moderate and easily manageable, these side-effects can become problematic in some cases. It is important to ensure good fluid intake and maintain a balanced diet. Your doctor may prescribe specific medication, which can help control your symptoms.

Thrombocytopenia

Thrombocytopenia means that you have a low-level of **platelets** in your blood. Platelets are blood cells that help the blood to clot. If the platelet count drops too far, it can cause bleeding.

Whilst being treated with Velcade, your platelet count may drop during the dosing days (days 1, 4, 8 and 11) but should rise again during the treatment break (days 12 to 21). If your platelet count gets too low your doctor may give you a platelet transfusion.

Your blood count will be monitored regularly, but you should watch out for signs of bleeding such as easy bruising and nose bleeds - tell your doctor straightaway if this happens.

Fatigue

Fatigue can occur quite commonly whilst receiving Velcade. The fatigue may be a result of **anaemia** (a low red blood cell count), which can be managed with blood transfusions or a growth hormone called **EPO (erythropoietin)**. Fatigue can also be managed through proper rest, nutrition, hydration and regular gentle exercise.

Low blood pressure

If you have a history of hypotension (low blood pressure), or are on drugs to help lower your blood pressure, you may need your medication altered whilst having Velcade treatment.

For more information see Myeloma UK's Infosheets on *Peripheral Neuropathy, Fatigue and Nutrition / Diet*. To order your free copies, contact the **Myeloma Infoline on 0800 980 3332**.

Ensuring a good fluid intake can help prevent hypotension whilst being treated with Velcade.

Peripheral neuropathy

Peripheral neuropathy means that the nerves in the hands, feet, arms or legs are damaged. This can cause numbness, tingling, increased sensitivity and pain

Neuropathy can also be caused by other myeloma treatments such as thalidomide and vincristine, and can also be caused by the disease itself. This can contribute to any peripheral neuropathy symptoms caused by Velcade.

Symptoms such as numbness, tingling and pain should be reported to your doctor or medical team as soon as possible. The best way to manage peripheral neuropathy is to reduce the dose of Velcade.

In the majority of cases symptoms will improve or disappear after the dose of Velcade is reduced. This is why it is important to tell your doctor about any symptoms promptly.

Velcade may need to be temporarily stopped or in more severe cases, discontinued and other options discussed.

Pain and discomfort can be alleviated by gentle massage, taking warm baths, using heat / cold packs and paying attention to posture. Nerve-related pain often requires specific pain-killing drugs which can be prescribed and monitored by your doctor.

Other interventions which have been reported to help symptoms of neuropathy included nutritional supplements such as vitamin B, folic acid and various amino acid supplements. However, these are not established treatments and should be discussed with your doctor.

The future

Velcade brings a new way of treating myeloma by attacking it in a different way to other treatments. This new mechanism of action has been shown to be effective at different stages of myeloma by improving response rates and survival compared with conventional chemotherapy.

In addition, the side-effect profile appears to be generally manageable. This represents a major breakthrough for myeloma and brings with it new hope for the future.

Over the next few years it is likely that clinical studies will teach us more about the safest and best ways to use Velcade in myeloma, with studies already underway in newly-diagnosed patients and looking at different combinations.

Questions for your doctor / medical team

Top Tips

- Write your questions down and give a copy to your doctor at the beginning of your consultation.
- Carry a piece of paper with you to make a note of questions as they occur to you.

Some questions you may need answering include:

- Would Velcade help me?
- What are the aims of treatment with Velcade?
- Are there any alternative treatments?
- Is Velcade appropriate for me to take at this stage of my disease?
- How experienced are you and your team in using Velcade?
- How long might I be on Velcade?
- What side-effects might I expect?
- What should I do if I experience any side-effects?
- Which side-effects should I report urgently and to whom?
- Is Velcade being given to me as part of a clinical study?
- What options are available if Velcade does not help or stops working?

Medical terms explained

Anaemia: A below-normal number of red blood cells in the blood. This reduces the ability of the blood to supply oxygen to the body, causing fatigue and weakness.

Clinical study: Research studies that involve people. Each study tries to answer scientific questions and to find better ways to prevent or treat cancer.

Conventional / standard treatment: The best treatment currently used based on results of past research.

Chemotherapy: Treatment with potent drugs intended to kill cancer cells. Chemotherapy can be injected into a vein (intravenous or IV) or swallowed as tablets (orally).

Erythropoietin (EPO): A hormone produced by the kidneys. Myeloma patients with damaged kidneys don't produce enough erythropoietin and can become anaemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency.

Haemoglobin: The molecule that carries oxygen around the body in red blood cells

Hypercalcaemia: A higher-than-normal level of calcium in the blood. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. Common in myeloma patients and usually resulting from bone destruction with release of calcium into the blood stream. Often associated with reduced kidney function since calcium can be toxic to the kidneys. For this reason, hypercalcaemia is usually treated on an emergency basis using IV fluids combined with drugs to reduce bone destruction together with direct treatment for the myeloma.

Immunoglobulins: Also known as antibodies, immunoglobulins are proteins found in the blood which are produced by cells of the immune system, called plasma cells. Their function is to bind to substances in the body that are recognised as foreign antigens and are found on the surface of bacteria and viruses.

Paraprotein: An antibody-like protein produced by the abnormal plasma cell in myeloma. It is found in the blood and sometimes also in the urine. It is also called monoclonal protein, myeloma protein, M spike, M protein or M band.

Plasma cell: Normal plasma cells are found in the bone marrow and produce antibodies to fight infection. In myeloma, the malignant plasma cells produce large amounts of a single abnormal antibody that does not fight infection. Malignant plasma cells also produce other chemicals which can result in organ and tissue damage.

Platelet: Platelets are a type of blood cell which are integral to the normal clotting mechanism of blood.

Side-effects: Problems that occur when treatment affects healthy cells. Common side-effects of standard cancer treatments are fatigue, nausea, vomiting, decreased blood cell counts, hair loss and mouth sores. New treatments being tested may have these or other unknown side-effects.

Further information and useful organisations

British Committee for Standards in Haematology (BCSH)

www.bcsghguidelines.com

The BCSH provides haematologists with up-to-date advice on the diagnosis and treatment of myeloma. Its website contains a range of position papers and guidelines relevant to those affected by myeloma, including the *Guidelines on the Diagnosis and Management of Multiple Myeloma*.

Cancer Research UK

www.cancerhelp.org.uk

Its website contains patient information on all types of cancer and gives details of current research and clinical studies.

Multiple Myeloma Research Foundation (MMRF)

www.multiplemyeloma.org

001 203 972 1250

The MMRF is a US based private funder of worldwide myeloma-specific research. Its website has information on myeloma treatments and international clinical trials.

NHS Direct / NHS24

www.nhsdirect.nhs.uk

In England, Northern Ireland and Wales call NHS Direct on 0845 46 47

In Scotland call NHS24 on 08454 24 24 24

Trained medical professionals provide 24-hour access to information on all aspects of health and healthcare.

National Institute for Health and Clinical Excellence (NICE)

www.nice.org.uk

NICE produces guidance on health technologies (the use of new and existing medicines, treatments and procedures) and clinical practice within the NHS.

Ortho Biotech

www.orthobiotech.co.uk

0800 731 8450 (Medical Information Department)

Ortho Biotech is the company that supplies Velcade in the UK.

UK Myeloma Forum (UKMF)

www.ukmf.org.uk

UKMF is an organisation of people professionally engaged in the field of myeloma who are working to improve the outlook for patients with myeloma and related disorders.

On behalf of the British Committee for Standards in Haematology, UKMF has produced guidelines on the diagnosis and management of myeloma.

With Myeloma UK you can...

Call our Myeloma Infoline on 0800 980 3332

You will immediately access information and support relating to all aspects of myeloma. Your call will be answered in confidence by Myeloma Information Nurse Specialists who are supported by medical and scientific advisors. Lines are open Monday to Friday, 9am to 5pm, and are free to phone from anywhere in the UK. From outside the UK call +44 131 557 3332 (charged at normal rate).

Contact us by email

If you have a specific question about any aspect of myeloma, treatment or living with myeloma, you can also contact our Myeloma Information Nurse Specialists by email at askthenurse@myeloma.org.uk

Order our free patient information

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets which give information on myeloma and related disorders, providing details of treatment options and disease management. You will find a list of the information available from us at the back of this Infoguide.

Attend our Patient and Family Myeloma Infodays

These are full-day meetings, where you can learn about the latest in the treatment and management of myeloma from a panel of experts. They are also a valuable opportunity to meet others affected by myeloma.

Subscribe to *Myeloma Matters*

The only myeloma-specific newsletter available in the UK, *Myeloma Matters* offers a fantastic range of features, articles and stories to help you keep abreast of the latest developments in treatment and research.

Visit our website - www.myeloma.org.uk

Developed to provide immediate, 24-hour access to information about myeloma and related disorders to individuals affected by the disease and to the people caring for them.

We need your help

Each year, Myeloma UK sends Infoguides and Infosheets to nearly 10,000 patients and their families, and helps thousands more through providing services such as the Myeloma Infoline and Patient and Family Myeloma Infodays.

That is why we need your help

We depend on the support and generous donations from people like you to provide these important services which are available free to myeloma patients, their families and carers.

Will you help us to help others?

- £5 will pay for an Infopack to be sent to help one more patient
- £20 will allow one of our highly trained Myeloma Information Nurse Specialists to help two callers on our Myeloma Infoline
- £50 will pay for a family of three to attend a Myeloma Infoday
- £250 will pay for 2,000 patient information Infosheets

Simply choose the amount that is right for you, or, if you prefer, choose an amount of your own. To donate you can either post your donation (by cheque or CAF), use your credit card to donate by telephone or use the Myeloma UK website www.myeloma.org.uk

We can make your money go further if you are a UK taxpayer. If you pay tax at the basic rate we can claim 28p on every pound you donate. For example, if you donate £10 then we are able to claim back £2.80, so your donation becomes £12.80. This extra comes from the taxman and doesn't cost you anything. This process is called Gift Aid.

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Other information available from Myeloma UK

Booklets

Myeloma – Your Essential Guide
Living with Myeloma - Your Essential Guide

Infoguides

Balloon Kyphoplasty
Bone Disease and Bisphosphonates
Clinical Studies
High-Dose Therapy & Stem Cell Transplantation
MRC Myeloma IX
Percutaneous Vertebroplasty
Revlimid
Serum Free Light Chain Assays
Thalidomide

Infosheets

Infosheet topics include:
Chemotherapy; Erythropoietin; Fatigue; Growth Factors; Managing Your Finances (including Benefits); Mouthcare; Nutrition / Diet; Radiotherapy; Peripheral Neuropathy; Plasmapheresis; Steroids; Support Groups; The Kidney; Travel Insurance; Travelling

Leaflets

Myeloma – An Introduction

There are a number of conditions closely associated with myeloma. Myeloma UK has information available on AL amyloidosis, Waldenström's macroglobulinaemia and MGUS.

To order these free publications please contact Myeloma UK.
Myeloma Infoline: 0800 980 3332 (freephone number) or 0131 557 3332
www.myeloma.org.uk email: myelomauk@myeloma.org.uk

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www.myeloma.org.uk
Infoline 0800 980 3332



For more information or to access any of the information and support services listed, contact Myeloma UK

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