



Understanding multiple myeloma and its treatment

Information for patients with multiple myeloma

Johnson & Johnson

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Introduction

When someone is first diagnosed with multiple myeloma, it can often lead to feelings of anxiety and anger. These feelings can be made worse by a lack of information, so it is important that you get a good understanding of multiple myeloma and its treatment.

Knowledge can help you tackle the disease and deal with it every day. It's the first step towards effective treatment.

We intend the information in this booklet to give you an overview of the disease and provide answers to the most commonly asked questions. Remember, though, that your haematologist should be the first person you talk to about more specific queries.

What is multiple myeloma?

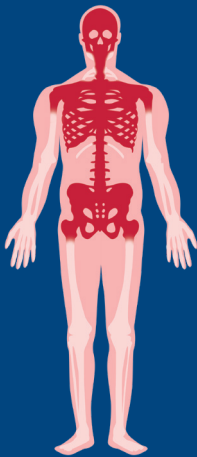
Each healthy cell in the body follows certain rules, it:

- multiplies only when needed
- changes when necessary
- dies when the body requires it.¹

Unfortunately, a cancer cell does not follow these rules, it:

- multiplies at the wrong time
- multiplies in the wrong place
- does not develop in the way needed to perform its proper function.¹

Multiple myeloma is a cancer of plasma cells – a type of white blood cell in the bone marrow that makes antibodies. A cancerous or malignant plasma cell is called a myeloma cell.^{2,3} Multiple myeloma can appear as a tumour, an area of bone damage, or both. Bone damage is referred to as 'lesions'. Multiple myeloma affects the places where bone marrow is active in an adult.^{2,3}



Myeloma is called 'multiple' because there are often multiple areas in the bone where it grows.^{2,4}

Myeloma most often grows in the marrow of bones located in the:^{2,4}

- spine
- skull
- pelvis
- rib cage
- areas around the shoulders and hips

Usually, the bones of the hands, feet and the lower portions of the arms and legs are unaffected.⁴

The accumulation of myeloma cells in the bone marrow results in the following medical issues:



The release of calcium from damaged bone into the bloodstream can result in:

- thirst
- nausea
- vomiting
- confusion
- constipation.^{2,4}



The overproduction of an abnormal antibody called M-protein can slow blood circulation and damage the kidneys.^{2,3}



An imbalance in the body's bone-forming and bone-destroying cells (osteoblasts and osteoclasts) can lead to the bones becoming weak and damaged.^{3,4}



A decrease in the number of red blood cells produced can cause anaemia, resulting in weakness and tiredness.^{2,3}



A decrease in the number of white blood cells can leave patients susceptible to infection, and delay their recovery from infections.^{2,3}

Diagnosis and tests

There are a few ways to test for multiple myeloma. Your condition may have been diagnosed through one or a combination of the following:

Blood test²⁻⁴

Multiple myeloma is often discovered from a blood test. The main test for the condition is a type of analysis called 'electrophoresis'. This is done on the proteins in the blood. It can show whether or not there is too much immunoglobulin (antibodies) in the blood. Higher than normal levels suggest someone has multiple myeloma.

Electrophoresis can also test your urine. This is because a part of the immunoglobulin can often be found there.

A blood test can also be used to find out:

- what level of anaemia you have
- if your blood platelets are 'deficient' (do not clot normally)
- if your kidneys are working normally
- what your calcium levels are.

All these things help to confirm a diagnosis and suggest the best course of treatment.

Imaging techniques for myeloma^{2,4}

An X-ray of the bone can help to identify changes in the bone and if there are cavities in the bone (called bone lesions). The most frequent parts of the body X-rayed are the:

- skull
- spine
- humerus bones in the arms
- the thigh bones.

Other imaging techniques may also be used, like:

- magnetic resonance imaging (MRI)
- a CT (computed tomography) scan
- a PET (positron emission tomography) scan.

These are more sensitive than an ordinary X-ray, and can also detect any impact the disease is having on other organs.

Bone marrow analysis²⁻⁴

Bone marrow can be analysed by either:

- drawing a small amount of bone marrow fluid (aspiration); or
- surgically removing a small amount of tissue (biopsy).

Both of these types of samples are usually taken from the hipbone using a large needle. These tests can determine the presence and extent of cancerous cells in the bone marrow.

The samples can also undergo 'cytogenetic testing'. This is done by a process called FISH – fluorescence in-situ hybridization. It can identify specific alterations in the DNA of the myeloma cells.

This is useful, because the test may show genetic changes that suggest a more aggressive disease that needs specific treatment.

Classifying and staging multiple myeloma

You may have heard myeloma referred to as having:

- different classifications
- different stages.

These are two different things.

Classification

- Classification refers to the type of myeloma.

Staging

- The stage reflects the extent of the disease.

Both classification and staging help to determine the most appropriate treatment.

Classification

Monoclonal gammopathy of unknown significance (MGUS)^{4,5}

If you have MGUS it means that there is a very low level of M-protein in your bone marrow, but it has not caused you any symptoms or damaged any of your organs.

This is common and happens in three to four out of every 100 people over the age of 50. The incidence increases with age.

While MGUS can develop into active myeloma, this is rare. It is considered to be a slight biological abnormality and tends to be monitored rather than treated.

Solitary plasmacytoma^{3,4,6}

In rare cases, a single lesion (group of malignant myeloma cells) is seen. This is often in the bone and without signs of bone marrow abnormalities. Various treatments are possible, but radiotherapy is often preferred.

Asymptomatic or smouldering/indolent myeloma^{4,5}

Asymptomatic, smouldering/indolent myeloma is when:

- low levels of M-protein are found in your blood; or
- there are more than 10% plasmocytes in your bone marrow.

And with this condition there is:

- no sign of damage to the organs
- no anaemia
- no bone lesions
- no hypercalcaemia
- adequate kidney function.

In most cases, patients with asymptomatic smouldering/indolent myeloma do not require any treatment. However, it is essential that you are monitored to make sure it does not progress. Sometimes, additional tests show that you are at an increased risk of quickly developing more serious myeloma. In that case your doctor can consider starting treatment immediately.

Active or symptomatic myeloma³

With active or symptomatic myeloma, it means that as well as abnormal proteins and malignant plasma cells that are present in your bone marrow, you have damage to your bones and various organs, for example the kidneys.

Staging^{2,3}

It is essential to stage myeloma to set up appropriate treatment. The most common way to stage myeloma is by using the International Staging System (ISS). It looks at the levels of specific blood proteins and takes into account individual genetic traits to classify myeloma at Stage 1, Stage 2 or Stage 3.

Your healthcare team

When you were diagnosed with multiple myeloma, you might have felt like you were more alone than ever before in your life. But apart from your family and friends, there is a team of healthcare professionals who are with you every step of the way.

Your multiple myeloma care team is known as 'multidisciplinary' because it includes specialists from different areas of medicine working together for your wellbeing. Understanding their roles and responsibilities may help you prepare specific questions you might want to ask during your treatment visits.



Primary care physician – your General Practitioner (GP)

Your GP was probably the first person you saw when you became ill. Even after your treatment gets under way, your GP may still be the first person you contact for any healthcare issues.

Oncologist and haematologist

Your GP will have referred you to a specialist in multiple myeloma who is either a medical oncologist or a haematologist. Oncologists are trained in the diagnosis and treatment of cancer, while haematologists are experts in diseases that affect the blood.

Radiation oncologist

You may be referred to a radiation oncologist. This is a physician who specialises in treating cancer with radiation therapy.

Orthopaedic surgeon

An orthopaedic surgeon is an expert in bone surgery and will be there to address any orthopaedic (bone-related) problems that you may have during treatment.

Oncology nurse

An oncology nurse is specially trained to work closely with your haematologist or oncologist to coordinate your care and give treatments.

Social worker

Social workers can help you with emotional, physical or financial problems. They can also advise you about any practical support services that may be available.

Psychiatrists and psychologists

Living with multiple myeloma can be tough and some might find it challenging at an emotional level.⁴ You may benefit from speaking with a professional counsellor, like a psychiatrist or a psychologist.

What is the difference between a psychiatrist and a psychologist?

A psychiatrist is a medical doctor trained to diagnose and manage mental illness. Psychiatrists can prescribe medication, such as antidepressants, if you need them.

A psychologist is not a medical doctor, but someone who is well trained in counselling and human psychology. They cannot prescribe medication.

Dietitians

Multiple myeloma and its treatment can make eating difficult. A registered dietitian can help you to maintain the healthiest diet possible throughout treatment.⁴ Your dietitian will be able to suggest foods or drinks to help if you are experiencing:

- nausea
- vomiting
- loss of appetite
- a dry or sore mouth.

Pharmacist

As well as dispensing medications, your pharmacist is a valuable source of information. They can answer questions about:

- when and how to take medicines
- what side effects to expect
- what to do if you have side effects.

Dentist

Since myeloma affects your bones, your jaw and teeth may be affected too.⁴

If your dentist is not already familiar with the special needs of people with multiple myeloma, you should tell them about your medication or pass on the details of your specialist so that any necessary treatments can be planned properly.



The goal of treatment

Although we are still working towards a cure for multiple myeloma, treatments are more effective than they have ever been.^{2,4}

The goal of multiple myeloma treatment is three-fold:^{2,4}

- ✓ To stop or slow the progression of myeloma.
- ✓ To encourage and prolong the periods where symptoms partially or completely disappear – known as remissions.
- ✓ To improve your quality of life – for example by relieving symptoms.

Even though many treatments successfully achieve some or all of these goals, for most people with multiple myeloma, the disease has a high **relapse** rate. This means signs and symptoms of myeloma can suddenly reappear after a period of improvement.^{2,4} This can be a sign that a patient is no longer sensitive to a particular therapy. If this is the case, the disease is said to be **refractory** to this treatment.⁴

Effective treatments:

- prevent relapse
- reduce complications
- help people to live as long as possible.^{2,4}

Reducing complications means:

- limiting the impact the cancer has on the body
- stopping the cancer from spreading
- keeping your bones strong, which will help you feel better for longer.²

Treatments for multiple myeloma

Treatments for myeloma can be broadly classified into the following groups:^{2,7}

- Anti-myeloma drugs
- High-dose chemotherapy and autologous transplantation
- Allogenic transplantation
- Standard chemotherapy

Depending on the myeloma you have and your general health and fitness, you will receive some or all of the options below. Often, more than one of these options are combined to achieve maximum effect.^{2,4} Typical combinations of these therapies are detailed below.

All drugs mentioned in this booklet are referred to by their 'generic' drug name, which is the scientific name of the actual active ingredient. However, every drug also has one or several brand names that you might hear a doctor or nurse using instead. If you don't recognize the name of the treatment(s) you've been prescribed, ask your doctor or nurse for clarification.

Brand names start with a capital letter, and often include an ® symbol after the name. The generic name often appears afterward in lower case, and may be included in brackets.

1) Anti-myeloma drugs

Newer types of medication have been developed in recent years. The combination of these treatments has contributed to more powerful effects on the myeloma and has significantly prolonged length of survival.⁸ These medications can be divided into four major categories:

Proteasome inhibitors (PIs)⁷

In a normal cell, proteins are broken down by a small structure known as a 'proteasome'. This acts like a waste bin where used proteins are recycled.

Cancer cells, which have increased metabolism, use these proteasomes very intensively to keep functioning.

Various medicines have been developed that are specially designed to keep these waste bins shut. This makes the used proteins gather in the cancerous cells and eventually the cells die. Examples of these medications include:

- bortezomib
- carfilzomib
- ixazomib.

Immunomodulators (IMiDs)^{7,9}

These drugs have a direct effect on cancer cells, and they also regulate certain parts of the immune system. They can activate certain immune cells and prevent certain types of growth signals for cancer cells.

By 'modulating' the immune system in this way, they use the body's own defense mechanisms against the cancer.

Examples of IMiDs include:

- lenalidomide
- pomalidomide

Monoclonal antibodies (mAbs)^{7,10}

These antibodies are used as immunotherapy to activate the body's own immune system to eliminate cancer cells. These antibodies are highly targeted, attaching to particular proteins located on the wall of the tumour cells. As a result, the immune system recognises these cells and they are attacked. Examples include:

- daratumumab
- elotuzumab
- isatuximab

Other products

Corticosteroids have long been used in myeloma treatment due to their ability to kill myeloma cells in high doses. Examples include prednisone and dexamethasone. They are often used in combination with other anti-myeloma drugs.^{7,11}

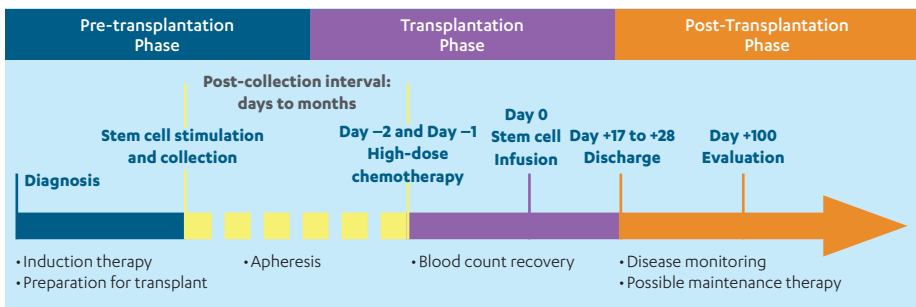
2) High-dose chemotherapy and autologous transplantation^{12,13}

One of the problems of chemotherapy is that when given in high doses it destroys stem cells in the bone marrow. These are the cells that go on to develop into blood cells, and are therefore essential for maintaining good health.

A solution is to collect a sample of stem cells from a patient before the high-dose chemotherapy so that they can be given back to them afterwards.

Because it's the patient's own cells being given back to them, it is called an 'autologous' stem cell transplant.

The process is as follows:



Induction therapy

This is initial therapy designed to remove the majority of myeloma cells from a patient's system.

Stem cell collection

Stem cells are the cells from which all blood cells – red blood cells, white blood cells and platelets – develop. After induction therapy, patients are given a 'growth factor' – a synthetic form of a naturally occurring substance that stimulates cell growth – stimulating the growth of stem cells for 5 to 7 days. This makes the stem cells enter the bloodstream, and these can be collected by a process called 'apheresis'.

Apheresis

To gather the stem cells, blood is taken from one arm and run through an apheresis machine that separates the blood cells. The stem cells are collected to be sent to a laboratory where they are treated and frozen for later use. The rest of the blood is returned through the other arm. An apheresis session takes about 4 hours and is performed in an outpatient setting or with a brief hospital admission.

High-dose chemotherapy

After the stem cells are collected, patients receive a high dose of chemotherapy (usually melphalan). This is highly toxic. Significant side effects include:

- infections
- digestive disorders
- total loss of appetite
- sore mouth
- diarrhoea
- bleeding
- hair loss.

You will need to be in hospital for 2 to 3 weeks to limit and counteract these risks.

Stem cell infusion

Once the high dose chemotherapy is over, the previously collected stem cells are re-introduced into the patient's body. The process by which the stem cells allow the patient's blood count to recover is called 'engraftment'.

It takes around 10 to 14 days before enough blood cells have been produced by the transplanted stem cells.

3) Allogenic transplantation¹³

In this type of transplantation the stem cells come from another person: a compatible donor – usually a brother or sister.

Allogenic transplants aim to use the immune system of the donor to help fight the patient's myeloma.

However, these transplants are associated with risks. The most significant are that you will get an infection or that your body tissues will react badly to the transplanted cells from the donor.

4) Standard chemotherapy

These drugs are administered either orally or intravenously (through a drip). They aim to kill cancer cells.⁷ A key drug used in this context is **melphalan**, which is given orally and is generally tolerated quite well.¹⁴ Melphalan is also used as part of autologous transplantation, but in this context it is administered at a high dose intravenously.¹³

Other products used for chemotherapy include:

- cyclophosphamide
- doxorubicin
- vincristine⁷
- bendamustine.¹⁵

Follow up

During the treatment

You will have regular check-ups where you can report anything that you are worried about.² Do not hesitate to mention any symptoms even if you think they are minor, for example, gradual loss of feeling in your feet or hands. These symptoms often indicate peripheral neuropathy (nerve damage). In that case, the healthcare team need to adjust your treatment schedule.

Alongside the regular contact with your carers, you must contact your healthcare team to report any rise in temperature or any new bleeding. These symptoms need urgent treatment.

At the end of treatment^{2,4}

Your healthcare team will assess your treatment again based on:

- the abnormal proteins in your blood and urine
- an analysis of the bone marrow
- a magnetic resonance imaging scan of the bone, possibly supplemented by a PET scan and X-rays.

These examinations will show how complete your remission is. The more complete the remission, the longer it is likely to last.

After the treatment

On the basis of your test results (blood and urine), your doctor will let you know how often you will have to return for checks. It is important that you consult the doctor outside of these planned visits if you have any worrying symptoms, particularly a rise in temperature and pain. Do not wait until your next appointment.

References

1. Cancer Research UK. How cancer starts. Available at: www.cancerresearchuk.org/about-cancer/what-is-cancer/how-cancer-starts. Last accessed Aug 2018.
2. Myeloma UK. Myeloma: an introduction. Available at: www.myeloma.org.uk/wp-content/uploads/2018/03/Myeloma-UK-Myeloma-An-Introduction.pdf. Last accessed Aug 2018.
3. International Myeloma Foundation. Concise review of the disease and treatment options. 2017 edition. Available at: www.myeloma.org/sites/default/files/images/publications/UnderstandingPDF/concisereview.pdf. Last accessed Aug 2018.
4. Myeloma Patients Europe. Multiple Myeloma – A Patients’ Guide. Available at: www.mpeurope.org/files/Patients-guide-mpe-web-version-V2.pdf. Last accessed Aug 2018.
5. International Myeloma Foundation. Understanding MGUS and smoldering multiple myeloma. Available at: www.myeloma.org/sites/default/files/images/publications/UnderstandingPDF/u-mgus_smm.pdf. Last accessed Aug 2018.
6. Moreau P, et al. *Ann Oncol*. 2017;28 (Suppl 4):iv52–iv61.
7. Multiple Myeloma /research Foundation. Standard treatments. Available at: <https://themmr.org/multiple-myeloma/treatment-options/standard-treatments>. Last accessed Aug 2018.
8. Dimopoulos MA, et al. *Nat Rev Clin Oncol*. 2015;12:42–54.
9. Palumbo A, et al. *Blood*. 2008;111:3968–3977.
10. Myeloma UK. Isatuximab. Horizons Infosheet Clinical trials and novel drugs. Available at: <https://www.myeloma.org.uk/wp-content/uploads/2020/01/Myeloma-UK-Isatuximab-Horizons-Infosheet.pdf>. Last accessed Jul 2020.
11. NHS. Treatment: multiple myeloma. Available at: www.nhs.uk/conditions/multiple-myeloma/treatment. Last accessed Aug 2018.
12. Miceli T, et al. *Clin J Oncol Nurs*. 2013;17(suppl):13–24.
13. Myeloma UK. High-dose therapy and autologous stem cell transplantation. Available at: www.myeloma.org.uk/wp-content/uploads/2018/03/Myeloma-UK-HDT-SCT-Infoguide.pdf. Last accessed Aug 2018.
14. Esma F, et al. *Expert Opin Pharmacother*. 2017;18:1127–1136.
15. Bendamustine hydrochloride Summary of Product Characteristics, Jan 2018.

SE Reporting

If you experience any treatment-related side effects, talk to the doctor or nurse. Do not try to treat your symptoms on your own. You can also report side effects directly via the national reporting system listed below. In case of side effects related to a Janssen medicine, you can also report these via the below Janssen mailbox.

KSA:

SFDA (National Pharmacovigilance and Drug Safety Department)

Email: npc.drug@sfd.gov.sa

Tel: 19999

Fax: +966 11 2057662

Online: <http://ade.sfda.gov.sa>

UAE:

Ministry of Health and Prevention/Drug Department/ Pharmacovigilance and Medical Device section

Email: pv@mohap.gov.ae

Tel: 80011111

Website: <https://www.mohap.gov.ae/en/services/adverse-drug-reaction-reporting>

P.O. Box:1853 Dubai, United Arab Emirates

Kuwait:

Pharmaceutical and Herbal Medicine, Registration and Control Administration, Ministry of Health, Sulaibkhat - Jamal Abdel Nasser Street, PO Box 5 Zip Code 13001, Kuwait,

Tel: +96524815382,

Website: <https://eservices.moh.gov.kw/HSDrugComplaints.aspx>.

Oman:

Department of Pharmacovigilance & Drug Information MOH

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