



Myeloma Canada
InfoGuide Series

Multiple Myeloma Patient Handbook



MYELOMA CANADA

MAKING MYELOMA MATTER

www.myeloma.ca





Reviewers

Healthcare professional

Darrell White, MD, MSc, FRCPC, FACP
Canadian Myeloma Research Group (CMRG) Board Chair
Professor, Division of Hematology
Queen Elizabeth II Health Services Centre
Dalhousie University
Halifax, NS

Myeloma Canada wishes to acknowledge and thank the Myeloma Canada's Patient Advisory Council (PAC) and the many individuals in our community who provided their invaluable input.

Editors

Gabriele Colasurdo, MSc
Director, Science & Research
Myeloma Canada
Montreal, QC

Jessy Ranger
Director, Patient Programs,
Health Policy & Advocacy
Myeloma Canada
Montreal, QC

Marcie Baron
Director, Corporate Communications & Marketing
Myeloma Canada
Montreal, QC

Karine Gravel
Project Manager, Education & Patient Services
Myeloma Canada
Montreal, QC

The information in this Handbook is not meant to replace the advice of a medical professional. They are the best people to ask if you have questions about your specific medical/social situation.





A new journey



Hundreds of years ago, explorers set sail, uncertain of where they would end up or what they would encounter. Being diagnosed with multiple myeloma is similar in many ways. The life and world you have known has changed, and you are embarking on a journey in a new and often unfamiliar world. Sometimes it may seem overwhelming and frightening; however, there are people to help and support you. Some of them may be in your home, family and community; others may be at your hospital, cancer centre or place of worship. Myeloma Canada also has a national network of local support groups, virtual support groups, and peer-to-peer support programs that can help you in your journey.

In this Handbook we'll define what "multiple myeloma" is, as well as its underlying disease process. Some of the information may appear intimidating or complex at first. Don't worry, over time you will understand more and more. Refer to this resource frequently and don't be afraid to ask your healthcare team for explanations.

Living with myeloma can be challenging and each person's experience is unique to them. Remember that you are never alone. Around the world, patient groups, healthcare professionals and researchers are working hard to improve the outlook for people living with myeloma. While we may not yet have a cure, the future is promising. Tremendous breakthroughs in drug therapies and treatments are enabling people with myeloma to live longer, with a better quality of life than ever before.





Introduction

Myeloma Canada's Multiple Myeloma Patient Handbook has been designed specifically for people living with myeloma, their families and their caregivers. The goal of this Handbook is to educate myeloma patients and their loved ones so they can become more active partners in their care.

If you have been searching for information on myeloma, you know how complicated it can be. This resource will attempt to give you accurate, reliable and clear information on myeloma, its potential causes and effects, and how it is diagnosed, staged and treated in Canada.

There is a lot of information in this Handbook and the more times you refer to it, the easier it will be for you to understand it. Over time, you will become more familiar with the disease, your treatment options, and what you can do to optimize your quality of life.

Some of the more technical or unusual words in this Handbook appear in ***bold italics*** the first time they're used and are explained in the **Glossary** starting on **page 45**. Don't be afraid to ask members of your or your loved one's healthcare team to explain any terms or concepts you may have trouble understanding.

Throughout your journey with myeloma, your healthcare team will provide you with a large amount of information about your potential treatment options, the disease itself, and more. Early identification, assessment and the treatment of symptoms is key. You may find it helpful to write down any questions you have along the way and share these with your healthcare team regularly. They are the best people to help you understand what is happening and guide you to make informed decisions.

Be an informed and cautious information consumer

Be cautious of information that comes your way. While books and the internet offer a wealth of information, not all of it is correct, it may not apply to your unique situation, and it may be confusing or misleading. Well-intended people may also try to offer you health advice without knowing the details of your condition and its treatment. Certain online support groups may also be helpful, but again be wary of possible misinformation. It's important to know that your source is reputable and to discuss what you read with your healthcare team. Never make any change to your treatment plan without checking with them first, and discuss any symptom you're experiencing.

To ensure you have the most reliable, up-to-date information and resources, visit the Myeloma Canada website, myeloma.ca often. There you will also find helpful links to support groups and programs, educational events and videos, and more.





Table of contents

What is multiple myeloma? 1
Monoclonal gammopathy of undetermined significance (MGUS) 5
Asymptomatic or smouldering multiple myeloma (SMM) 6
Symptomatic or active multiple myeloma 7
Diagnosing myeloma 10
Understanding treatment 15
Myeloma relapse 17
Overview of myeloma treatments 19
Treatment options for newly diagnosed patients (First-line therapy) 23
Treatment options at relapse (Second-line therapy and beyond) 25
Managing complications and side effects 27
Your healthcare team 34
Development, approval and reimbursement of new and emerging therapies 38
How to be your own advocate 42
About Myeloma Canada 43
Beyond family and friends: Myeloma support groups and programs 44
Glossary 45





What is multiple myeloma?

Overview

Multiple Myeloma is a cancer of the ***plasma cells***. The word "multiple" is often used because myeloma cells usually affect multiple areas of the ***bone marrow***. In this resource, we'll use the term "myeloma" to keep things simple. While a cure for myeloma has yet to be developed, scientific breakthroughs have resulted in more available treatment options, so that people with myeloma are living longer and with better quality of life. In fact, for many people myeloma has now become more of a chronic disease.

Myeloma and its pre-cursors, ***monoclonal gammopathy of undetermined significant (MGUS)*** and ***smouldering multiple myeloma (SMM)***, are a group of conditions and diseases that fall under the category of plasma cell disorders. In a nutshell, a plasma cell is a type of white blood cell (WBC) produced in the bone marrow, the "blood factory" located within the hollow area of bones, that produces ***antibodies*** to fight infection. Myeloma is the 2nd most common form of ***hematologic (blood)*** cancer; it may also be referred to as a cancer of the immune cells.

Abnormal accumulation of myeloma cells in your bone marrow have direct and indirect effects on your blood, bone and kidneys. Myeloma's signs and symptoms are often vague and thus are attributed to aging or other more common causes or conditions. People with myeloma may start noticing symptoms such as:

- Elevated blood calcium (hypercalcemia)
- Kidney (renal) damage
- Low ***hemoglobin*** (anemia)
- Persistent bone pain and/or fractures (lesions)
- Frequent or recurring infections
- Fatigue, weakness, shortness of breath

Myeloma is difficult to diagnose without an evaluation and work up by a hematologist/oncologist.

For more information on plasma cell disorders, please consult Myeloma Canada's MGUS and Smouldering Multiple Myeloma InfoGuide.

Blood cells

Three types of blood cells are made in the bone marrow:

1. ***Red blood cells (RBCs; erythrocytes)*** that carry oxygen.
2. ***Platelet cells (thrombocytes)*** that help the blood to clot whenever you cut yourself.
3. A variety of white blood cells (WBCs; leukocytes), including ***lymphocytes*** that play important roles in the functioning of the ***immune system***. Another variety of white blood cell you may hear of is neutrophil. This type of cell plays an important role in protection from infection. If you have a low neutrophil level you are more susceptible to infection.

There are two types of lymphocytes:

- T cells - "T", in T cell (or T lymphocyte), stands for thymus, the principal organ for their development.
- ***B cells*** (or B lymphocytes) are found in the bone marrow. As they mature, B cells turn into plasma cells.

Antibodies (immunoglobulins)

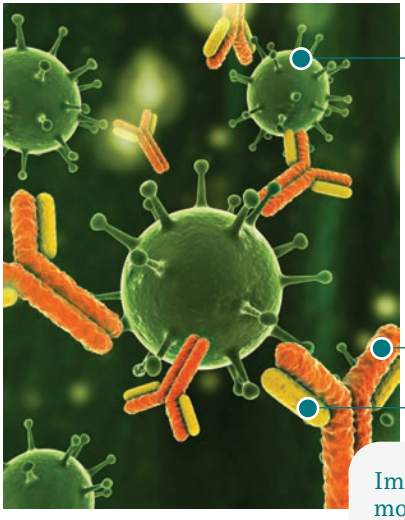
When plasma cells are exposed to foreign substances ***(antigens)***, they produce different antibodies. These antibodies are called ***immunoglobulins*** (abbreviated as Ig).

Immunoglobulins are proteins made up of two types of chains **(Figure 1)**:

- Heavy chains (G, A, M, D or E type)
- Light chains (kappa [κ], or lambda, [λ])

Normally, the most common immunoglobulin in the blood is ***IgG***, followed by ***IgA*** and ***IgM***. ***IgD*** and ***IgE*** are usually present in the blood in very small amounts.

Figure 1: Structure of an antibody (immunoglobulin)



Immunoglobulins (antibodies) are Y-shaped molecules. The heavy and light chains of the antibody contain specific binding sites that attach to bacteria or viruses, ultimately leading to their destruction thereby protecting against disease.

What happens when you have myeloma?

In myeloma, the B lymphocyte (the cell that matures into a plasma cell) is damaged. It begins to reproduce plasma cells uncontrollably. We commonly refer to this "good cell gone bad" as being "cancerous" or "malignant".

When plasma cells reproduce uncontrollably, two things happen:

1. The abnormally high number of plasma cells can "crowd" out other types of blood cells you need to be healthy (e.g., RBCs or platelets). In healthy people, plasma cells make up 2-3% of the cells in the bone marrow. In someone who has myeloma, plasma cells usually make up at least 10% of the cells – or even more.
2. Too much of the same type of antibody (immunoglobulin) is produced (i.e., too much IgG or IgA). This is referred to as ***monoclonal protein*** (M-protein), monoclonal spike (M-spike), monoclonal peak (M-peak), or paraprotein. All of the terms are interchangeable.

As myeloma cells multiply, they attach to other structural cells in the bone marrow known as stromal cells. Once attached to stromal cells, interactions occur that stimulate the myeloma cells to continue reproducing.

- Chemical messengers called ***cytokines*** are produced and stimulate the growth of myeloma cells and prevent them from dying naturally. ***Interleukin 6 (IL-6)*** is one of these chemical messengers.
- As more and more myeloma cells grow and multiply within the bone marrow, little space is left for your healthy immune cells to grow, and the immune system begins to weaken. Ordinarily your immune system would try to clear out or stop the growth of abnormal cells, but as the immune system weakens, it is unable to detect and battle all of the abnormal cells.

Myeloma cells can also invade bone and cause multiple areas of damage that weaken the bone. These areas are known as osteolytic lesions, or ***lytic bone lesions*** for short.

Sometimes, myeloma cells collect in a single bone and form a ***tumour*** called a ***plasmacytoma***. Occasionally, a plasmacytoma can affect areas of soft tissue outside of the bone ***(extramedullary plasmacytoma)***.

Incidence and prevalence of myeloma in Canada

Multiple myeloma is the second most common blood cancer in Canada. It remains incurable, for now, but thanks to tremendous strides and investments in research, new and innovative drug therapies and ***immunotherapy*** treatments are paving the way for people with myeloma to live longer and enjoy a better quality of life.

The Canadian Cancer Society's Canadian Cancer Statistics Advisory Committee reported an estimated **4,000** new diagnoses of multiple myeloma in Canada in 2022, which amounts to approximately eleven Canadians diagnosed every day. Biological males have a slightly higher risk of developing myeloma than biological females and the disease is more common in people of African ancestry. The reasons for these increased risks are unknown.

While myeloma is more prevalent in older adults, it is not just an older person's cancer. People in their 30's through to their 90's are receiving myeloma diagnoses. Given that the Canadian population is ageing, and people with myeloma are living longer thanks to new, more effective treatments, the prevalence of myeloma is increasing.

Another Canadian Cancer Society report determined the prevalence of multiple myeloma, as of 2022, to be **1 in 2,505** Canadians affected by the disease. Comparatively, more Canadians are living with myeloma in 2022 than with better-known cancers such as liver cancer (1 in 5511), pancreatic cancer (1 in 5011), and esophageal cancer (1 in 7397). Despite this, and its rising prevalence, myeloma remains a widely unknown cancer to the unaffected general public. Canada's national incidence and prevalence rates for myeloma are on the higher end, though consistently quite similar to those of other Commonwealth countries such as New Zealand and Australia, and the United States.

There is still much to learn about what causes myeloma. Studies have shown that environmental factors, including exposure to toxic chemicals (e.g. petroleum products, heavy metals, herbicides, insecticides, and dusts such as asbestos) and radiation, may be associated with a greater risk of myeloma. Similarly, excess body weight (obesity) has been shown to cause changes in the body that can increase your risk for several types of cancer, including myeloma. Moreover, certain occupations (e.g. agriculture, machinery production, carpentry and leather industry workers, as well as firefighters) carry a higher-than-average risk for developing myeloma.

For the most up-to-date statistics on myeloma, visit our website at myeloma.ca. There you'll find the most current information and data.

More information

Incidence vs. Prevalence

Incidence refers to the total number of new myeloma cases diagnosed in a given year. Prevalence describes the total number of people living with myeloma at a specific time.





Is myeloma an inherited cancer?

Studies have shown that some ***genetic*** variations can increase the likelihood that a person will develop myeloma. Although the effect of inherited genetic variations on developing myeloma is very small, some people may inherit a combination of genetic variations that puts them at higher risk of developing the disease. Overall, inherited factors are only a small part of the puzzle – other genetic and environmental risk factors are usually encountered before myeloma develops.

People with an immediate family history (parent, sibling, or child) of myeloma, or one of its precursor conditions, have a higher risk for developing myeloma or a precursor condition (e.g., monoclonal gammopathy of undetermined significance [MGUS]). Immediate family members have approximately double the risk of eventually developing myeloma compared to people with no family connection.

This might sound alarming but it's important to understand that, on the whole, the chance of developing MGUS or myeloma remains very low and the chance of MGUS progressing to active disease (i.e., multiple myeloma) is also very low.

What can you do right now if there is a history of myeloma in your family?

We recommend letting your family doctor know about your family medical history so that he/she can log it in your chart. That way, if your routine blood test shows an increase in blood protein they can order the appropriate follow-up tests, like:

- complete blood count (CBC)
- serum protein electrophoresis (SPEP) with immunofixation electrophoresis (IFE)
- 24-hour total urine protein with electrophoresis (UPEP) and IFE
- serum free light chain (sFLC; Freelite) assay

Please refer to the MGUS and Smouldering Multiple Myeloma InfoGuide for a full list of screening tests.





Monoclonal gammopathy of undetermind significance (MGUS)

MGUS is the earliest state of myeloma and is often referred to as a pre-cursor condition. In the majority of cases, MGUS does not cause symptoms (asymptomatic) and does not require treatment. In someone with MGUS:

- There may be more plasma cells than normal in the bone marrow, but it is still less than 10% of all blood cells (part of the definition of myeloma includes 10% or more plasma cells).
- M-protein level in the blood is usually less than 30 g/L .
- There is no ***anemia*** (low blood hemoglobin), ***renal insufficiency*** (kidney disease), ***hypercalcemia*** (elevated levels of ***calcium*** in the blood) or bone damage (lytic lesions) caused by the plasma cell disorder.

The prevalence of MGUS increases with age. It is observed in almost 3% of people aged 50 years or older and in approximately 5% of people aged 70 years or older. MGUS is relatively rare in people less than 40 years of age with a prevalence of less than 0.3%.

Why is MGUS important? People with MGUS have approximately 1% chance per year of developing active myeloma. Currently, there is no clear way to predict who will progress to active myeloma.







Asymptomatic or smouldering multiple myeloma (SMM)



SMM is the intermediate transitional state between MGUS and myeloma. Like MGUS, SMM is typically an asymptomatic condition that is usually observed but not treated. Compared to MGUS, SMM carries a higher risk of progression to myeloma – with an individual risk of approximately 10% per year for the first 5 years, 3% per year for ther next 5 years, and 1-2% per year for the next 10 years.

In SMM:

- Plasma cells may make up 10-60% of the bone marrow.
- M-protein level in the blood is greater than 30 g/L.
- M-protein level in the urine is equal to or greater than 500 mg per 24 hours.
- Like MGUS, there is still no anemia (low blood hemoglobin), renal insufficiency (kidney disease), hypercalcemia (elevated levels of calcium in the blood) or bone damage (lytic lesions) due to the plasma cell disorder.

Clinical trials are studying whether some people with high-risk SMM should begin treatment before the onset of active myeloma. Some have demonstrated a benefit to early treatment but this must be weighed against the potential side-effects of those treatments.





Symptomatic or active multiple myeloma

Symptomatic or active multiple myeloma is characterized by the presence of M-protein in the blood or urine and an increased number of plasma cells in the bone marrow. Active myeloma requires treatment.

People with active myeloma may develop complications called the "CRAB" criteria:

- Calcium elevated in the blood – hypercalcemia
- Renal insufficiency – kidney damage
- Anemia – low levels of hemoglobin in red blood cells (RBCs)
- Bone lesions – bone pain and/or fractures
  Lytic lesions can appear on bone imaging tests (e.g., ***magnetic resonance imaging [MRI]***, X-ray). Lesions weaken the bone, cause pain, and increase the risk of fractures. Another possible sign of active myeloma is the growth of a plasmacytoma in the bone or soft tissue.

You may also hear the term **"SLiM"** in relation to myeloma. SLiM refers to a more in-depth diagnostic criteria that better identifies people with SMM who may require active myeloma treatment even if they are not experiencing CRAB criteria symptoms.

SLiM criteria include the following three ***myeloma defining events (MDEs):***

- Sixty percent (60%) or more myeloma cells in the bone marrow
- Light chains: Involved/uninvolved ***serum free light chain (sFLC)*** ratio of 100 or greater
- Magnetic resonance imaging (MRI): More than 1 bone lesion of at least 5 mm in size



Table 1: Key differences in diagnostic criteria for MGUS, SMM and myeloma

Diagnostic criteria	MGUS	SMM	Myeloma
% of myeloma cells in the bone marrow	Less than 10%	10-60% and/or meeting the M-protein criteria below	60% or greater or at least 10% plus one or more of the following MDEs: • CRAB symptoms • Involved/uninvolved sFLC ratio of 100 or greater • More than 1 ***focal lesion*** of at least 5mm in size by MRI
M-protein (blood)	**Blood :** Less than 30 g/L	**Blood :** At least 30 g/L and/or **Urine :** 500 mg/24 hours	• Levels can vary • May not be present/detectable
CRAB symptoms (end-organ disease)	No	No	• High calcium levels (serum calcium greater than 2.75 mmol/L) • Kidney damage (creatinine clearance less than 40 mL/min) or blood creatinine greater than 177 µmol/L) • Anemia (hemoglobin less than 100 g/L) • Bone lesions (one or more as shown by imaging)

Types of myeloma

The type of myeloma someone has is often referred to by the type of M-protein heavy chain (i.e., IgG, IgA, IgM, IgD, or IgE) and light chain (i.e., kappa [κ] or lambda [λ]) that is over-produced by their myeloma cells. The most common type of myeloma is IgG kappa.

Other types of myeloma are classified as follows:

- **Light chain myeloma (also known as Bence-Jones myeloma):** About 15-20% of people with myeloma have light chain myeloma. This type of myeloma produces M-protein with only the light chain portion of the immunoglobulin and thus lacks the heavy chain portion. Free light chain M-protein can accumulate in the kidneys and damage them. A 24-hour urine collection is usually required to measure and monitor light chain protein. Some laboratories, however, use a ***serum free light chain assay (Freelite)*** to detect and measure free light chains.
- **Oligosecretory myeloma:** When very small amounts of M-protein are produced by myeloma cells, it is called oligosecretory myeloma. Oligosecretory means that only small amounts of protein can be measured in the blood or urine – much less than would be expected based on the level of myeloma cells in the bone marrow. Sensitive measurement of M-protein with the Freelite test may be available in some centres and can be useful in monitoring this type of myeloma.
- **Nonsecretory myeloma:** Approximately 3% of all people with myeloma have nonsecretory myeloma. Nonsecretory myeloma means myeloma cells are present in the bone marrow but the level of M-protein in the blood or urine is so low that it is hard to measure. The disease cannot be diagnosed or tracked by the usual blood and urine tests; it can, however, be detected in the bone marrow or upon ***biopsy*** of bone lesions. Kidney problems associated with myeloma light chains are much less common in patients with nonsecretory myeloma.

Genetic sub-types of myeloma

Different genetic ***(DNA)*** abnormalities associated with myeloma can affect how the disease will respond to treatment. Genetic subtypes can be identified by analyzing myeloma cells in a bone marrow sample for their ***cytogenetics***. The two laboratory-based techniques most commonly used for myeloma cytogenetics are ***karyotyping*** and ***fluorescence in situ hybridization (FISH)***.

FISH analysis allows scientists to look at the genetic make-up of your myeloma cells, identify specific changes, and provide detailed information about your condition to your healthcare team. Some cytogenetic features are associated with a higher risk that your condition may respond less optimally to treatment. Some cytogenetic abnormalities common in myeloma are below. These are examples of alterations and changes that can happen to the genes within your plasma cell:

- ***Translocations*** – i.e., t(4;14), t(14;16), t(14;20);
- ***Deletions*** – i.e., del(17p), del(13q);
- ***Gains*** – i.e., gain(1q).

Genetic profiling will play an increasingly important role in the personalization of myeloma treatment.

Related disorders

Plasma cell disorders related to myeloma include:

- **Amyloid light-chain (AL) amyloidosis:** About 10–15% of people with myeloma will have or develop AL amyloidosis. In AL amyloidosis, a specific protein called amyloid can collect and cause damage in one or more organs, such as the kidneys or the heart.
  - For more information, please refer to Myeloma Canada's Amyloid Light Chain (AL) Amyloidosis InfoSheet.
- **Light chain deposition disease (LCDD):** LCDD is characterized by the deposition of light chains in various organs. Although LCDD is most frequently seen in the kidneys, deposits can also occur in the lungs, intestines, or eyes.
- **POEMS syndrome:** POEMS is an extremely rare syndrome caused by an abnormal immune response that accidentally attacks normal cells in the nervous system. Common symptoms include progressive nerve weakness in the arms and legs, abnormally enlarged liver and/or spleen, enlarged lymph nodes, darkening and thickening of the skin, and excessive hair growth.
- **Waldenström macroglobulinemia:** The uncontrolled production of IgM can be a rare plasma cell disorder known as Waldenström macroglobulinemia, a type of non-Hodgkin lymphoma. It is marked by the presence of a high level of IgM M-protein and blood ***hyperviscosity***.





Diagnosing myeloma

Most people in the early stages of myeloma do not experience any symptoms. Often, they are unaware that what or how they may be feeling is however, a symptom of the disease. Most first go to their doctor because of fatigue, recurrent infections or back pain. Common symptoms of myeloma can include any of the following:

Symptom	Why it occurs
Pain in the lower back, ribs or sternum	Bone lesions weaken the bone and result in tiny fractures or the collapse of a vertebra in the spine. About 70% of people with myeloma seek medical attention because of pain related to bone lesions.
Fatigue	The increased number of myeloma cells can decrease the production of red blood cells and lead to anemia. Anemia is present in almost 75% of newly diagnosed people with myeloma.
Recurrent infections	Due to crowding in the bone marrow, the production of a variety of infection-fighting white blood cells is reduced. The immune system is therefore unable to adequately fight off infections and illness.
Tiredness accompanied by other symptoms such as thirst, frequent urination, nausea or muscle weakness	The breakdown of bone releases excess amounts of calcium into the blood (hypercalcemia). Hypercalcemia can result in a number of symptoms, such as loss of appetite, fatigue, muscle weakness, restlessness, difficulty in thinking, confusion, constipation, increased thirst, increased urine production, nausea and vomiting.
Kidney problems	Excessive protein in the blood (which is filtered through the kidneys), excessive light chains in the urine, or elevated levels of calcium in the blood can cause kidney damage.

Diagnostic or ***prognostic*** lab tests for myeloma involve testing the blood, urine and bone that help:

- establish whether M-protein is present in the blood or urine;
- confirm the presence of myeloma cells in the bone marrow;
- determine whether or not there is organ damage as a result of myeloma (e.g., bone damage or kidney dysfunction).

Blood tests

Complete blood count (CBC)

A complete blood count (CBC) measures the number of white and red blood cells in your blood as well as the number of platelets. When studying the results of a CBC, your doctor will look for decreased levels of:

- red blood cells or hemoglobin (an indication of anemia)
- platelets (referred to as thrombocytopenia)
- white blood cells (referred to as leukocytopenia)

Although values can vary, normal CBC results are summarized in the following table. Values that are significantly outside of the normal range will raise questions and may lead to other tests.

Table 2: CBC reference values in healthy individuals

Count	SI units*	Traditional units*
Erythrocytes (Red blood cells, RBCs)	**Female:** 4.2 – 5.4 x 10^{12}/L **Male:** 4.6 – 6.2 x 10^{12}/L	**Female:** 4.2 – 5.4 million/mm^3 **Male:** 4.6 – 6.2 million/mm^3
Hemoglobin (Hb or Hgb)	**Female:** 120 - 160 g/L **Male:** 140 - 180 g/L	**Female:** 12.0 – 16.0 g/dL **Male:** 14.0 – 18.0 g/dL
Leukocytes (White blood cells, WBCs)	**Total WBC:** 3.5 – 12.0 x 10^9/L **Neutrophils:** 3,000 – 5,800 x 10^6/L **Lymphocytes:** 1,500 – 3,000 x 10^6/L **Monocytes:** 300 – 500 x 10^6/L **Basophils:** 50 – 250 x 10^6/L **Eosinophils:** 15 – 50 x 10^6/L	**Total WBC:** 3,500 – 12,000/mm^3 **Neutrophils:** 3,000 – 5,800/mm^3 **Lymphocytes:** 1,500 – 3,000/mm^3 **Monocytes:** 300 – 500/mm^3 **Basophils:** 50 – 250/mm^3 **Eosinophils:** 15 – 50/mm^3
Platelets	150 – 400 x 10^9/L	150,000 – 400,000/mm^3

**Please note that normal values may vary from lab to lab. The ranges are for reference only.*

Blood chemistry

A blood chemistry panel will also be conducted. These tests look for indications of :

- Increased levels of total protein in the blood
- Poor kidney function (renal dysfunction). Indicators include :
  - Increased ***creatinine clearance (and/or serum creatinine)***
  - Decreased ***albumin***
  - An elevated level of ***lactate dehydrogenase (LD or LDH)***
  - Imbalance (too high or too low) in electrolytes (sodium, potassium, chloride, bicarbonate)
- More bone breakdown than normal. Indicators are:
  - Hypercalcemia: Elevated elevated calcium level in the blood that occurs when calcium is released from the bone.
- Liver function. Following the kidney, the liver is the second most common organ affected by light chains. Liver function indicators include:
  - Increases in bilirubin (total and direct), alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), or prothrombin time (PT).

M-protein assessment

Specialized blood tests are ordered to confirm the diagnosis and determine what type of myeloma you have.

- Serum protein ***electrophoresis*** (SPE or SPEP) gives a picture of the level of various proteins in the blood. SPEP shows if there is a monoclonal peak or abnormal level of a particular immunoglobulin, as well as kappa (κ) and lambda (λ) free light chains.
- Immunofixation is a specialized type of electrophoresis that can identify the type of monoclonal paraprotein that makes up the M-spike seen by the SPEP.
- A quantitative immunoglobulin (QIg) test measures the levels of different types of immunoglobulins or antibodies in the blood (e.g., IgG, IgA and IgM).
- A serum free light chain assay (Freelite) can be used to measure the level of free light chains in the blood.

To learn more about blood tests, please refer to Myeloma Canada's Understanding Your Blood and Blood Tests InfoGuide.

Urine tests

When myeloma is suspected, urine tests can be used to:

- measure the amount of M-protein (i.e., free light chains kappa [κ] or lambda [λ])
- test for ***creatinine***, a waste product excreted by the kidneys

Urine protein electrophoresis (UPE or UPEP) checks for the presence of free light chains (M-protein) in the urine. A 24-hour urine collection test may be conducted to measure the amount of M-protein in the urine over one day. Similarly to SPEP, immunofixation can identify the type of M-protein seen on the UPEP test. UPEP can also look at features (i.e., albumin present in the urine) indicative of renal disease (e.g., AL amyloidosis or another related condition).

Bone tests

Bone marrow

Samples of bone marrow may be taken to check the number of plasma cells. There are two types of bone marrow sampling techniques. In both cases, samples are usually taken from the hip bone ***(aspiration)***.

- ***Bone marrow aspiration*** — a needle with a syringe attached is used to draw a sample of liquid bone marrow. As well as examining the sample under a microscope, the cytogenetics of the plasma cells can be studied.
- ***Bone marrow biopsy*** — a biopsy needle is inserted into the bone and rotated to force a tiny sample of solid bone tissue into the needle. A biopsy is usually performed when you are first diagnosed and may not need to be repeated.

Bone imaging

A variety of imaging techniques can be used to look for areas of bone thinning, lytic lesions, and fractures. Types of imaging tests include:

- Whole-body low-dose computerized tomography (WBLDCT): The first-choice initial imaging test for detecting bone disease.
- Whole-body magnetic resonance imaging (MRI): If WBLDCT or ***skeletal survey (full-body X-ray)*** are negative or unclear.
- MRI of the spine and pelvis: If whole-body MRI is not available.
- Whole-body fluoro-deoxyglucose positron emission tomography/computed tomography (FDG-PET/CT): If MRI is not available. This imaging test is widely available in most Canadian centres.
- Skeletal survey (full-body X-ray): X-ray is no longer the gold standard for detecting bone disease, due to its low sensitivity for detecting early lesions (when less than 30% of the dense outer surface (cortex) of the bone is destroyed. If available, newer and more sensitive imaging techniques are preferred.
- Bone density tests (a form of special X-ray): Monitors bone loss and checks for specific areas of damage.

To learn more about bone complications, read Myeloma Canada's Myeloma Bone Disease InfoGuide.

Staging myeloma

When myeloma is diagnosed, prognostic lab tests can:
- help determine tumour burden (severity of the disease);
- suggest how aggressive the myeloma is;
- characterize the genetic abnormalities (cytogenetics) of the myeloma cells.

Prognostic tests are not conducted to tell you whether or not you have active myeloma, but to learn more about the disease and how advanced it is (known as its "stage"). The Revised International Staging System (R-ISS) is the main system used to stage active myeloma.

R-ISS is based on the following measurements:
- Serum (blood) ***beta-2 microglobulin (ß2M)*** — β2M is a protein that is normally found on the surface of cells. A higher-than-normal level of this protein indicates inflammation somewhere in the body. It may also indicate some types of white blood cell (lymphocyte) disorders. A normal level of β2M in the blood is usually less than 2.5 µg/mL, depending on the laboratory. Levels of β2M correlate with myeloma tumour burden and fall with response to therapy.
- Serum (blood) **albumin —** The most common protein in the blood is albumin. The normal range for albumin is 35-50 g/L. Lower levels may be an indicator of kidney dysfunction.
- Serum (blood) **lactate dehydrogenase (LDH) —** LDH is an ***enzyme*** found in almost all cells. High levels of LDH are an indicator that cells have been damaged or destroyed, and thus may be used to monitor myeloma activity.
- **Chromosomal abnormalities (cytogenetics) —** Chromosomal abnormalities can be detected by using a test called fluorescent in situ hybridization (FISH) on a sample of purified plasma cells. Certain chromosomal abnormalities are called "high risk" because they are associated with more aggressive or harder to treat myeloma. Such abnormalities include:
  - del(17p) – a deletion of the short arm of chromosome 17
  - t(4:14) – translocation of chromosomes 4 and 14
  - t(14:16) – translocation of chromosomes 14 and 16

Table 3: The Revised International Staging System (R-ISS)

R-ISS stage	R-ISS Test
Stage I	ß2 microglobulin is less than 3.5 mg/L **AND** albumin is equal to or greater than 35 g/L **AND** no high-risk chromosomal abnormalities **AND** normal LDH level
Stage II	All possible combinations of R-ISS stages I and III
Stage III	ß2 microglobulin is equal to or greater than 5.5 mg/L **AND** presence of at least one high-risk chromosomal abnormality: del(17p), t(4;14), and t(14;16) **OR** high LDH level





Getting a second opinion

Once your doctor has provided you with a diagnosis and a treatment plan, and if your doctor is not familiar with myeloma, or has not seen many myeloma patients in its practice, you may wish to have another specialist review the plan. This is called getting a second opinion. While you may have complete confidence in your doctor, in certain circumstances it may be helpful to have another expert opinion. You may feel uncomfortable asking for a second opinion, but you have a right to do so.

For tips on how to exercise your right to a second opinion and to learn more about advocating for yourself or for others, please refer to Myeloma Canada's Advocacy Handbook on myeloma.ca.





Understanding treatment

Once the disease has been treated and is under control, people with myeloma can spend periods of time with few or no symptoms and experience relatively normal lives. Bear in mind, however, that myeloma is a very individual disease and not all people experience the same symptoms, response to treatment, and/or ***overall survival***.

A number of factors are considered before your myeloma is treated:

- Physical examination and diagnostic test results
- The stage (severity) of your disease
- Presence of prognostic indicators (eg, genetic mutations)
- Your age and general state of health
- Symptoms being experienced (eg, bone pain or fractures)
- Complications being experienced (eg, kidney disease, anemia or infections)
- Pre-existing health problems (eg, heart disease, diabetes)
- Previous treatments and how your myeloma responded to them
- New treatments available through clinical trials
- Your preference

Each person's case is assessed individually. What works for one person may not work for another. Regardless of the treatment, the goals are similar:

- Stop the production of myeloma cells
- Strengthen bones and prevent fractures
- Increase hemoglobin count and reduce fatigue
- Reduce the risk of infections
- Prevent kidney damage
- Promote your well-being and enhance your quality of life

Treatment is customized to each situation. The initial treatment is called ***first-line therapy***. If there is no response to treatment (refractory disease) or if the disease comes back (relapsed disease), the next treatment is called ***second-line therapy***. Depending on the specific case, treatment may combine various approaches:

- Observation
- ***Radiotherapy***
- Corticosteroids (steroids)
- Chemotherapy
- Stem cell transplantation



- Immunomodulatory agents (IMiDs)
- Proteasome inhibitors (PIs)
- Selective inhibitors of nuclear export (SINE)
- Immunotherapy
  - Monoclonal antibodies (MoAbs)
  - Chimeric antigen receptor (CAR) T-cell therapy
- New and emerging therapies being studied in clinical trials

Response to treatment

Below are common terms used by the International Myeloma Working Group (IMWG) to describe treatment response categories. The IMWG conducts research to improve outcomes for people with myeloma as well as creates consensus guidelines for the international myeloma community.

sCR (stringent Complete Response): Complete Response plus normal free light chain κ/λ ratio (≤4:1 or ≥1:2 for κ and λ patients, respectively) and an absence of clonal cells in the bone marrow by immunohistochemistry.

CR (Complete Response): No detectable monoclonal protein (M-protein) in the serum and urine by immunofixation, disappearance of any soft tissue plasmacytomas (extramedullary tumours) and 5% or less of (cancerous) plasma cells in the bone marrow.

VGPR (Very Good Partial Response): Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein less than 100 mg per 24 hours.

PR (Partial Response): 50% or greater reduction in serum M-protein and a reduction in 24-hour urinary M-protein of 90% or more, or to less than 200 mg per 24 hours. If serum and urine M-protein are unmeasurable, PR is defined as a 50% or greater decrease in the difference between involved and uninvolved free light chains. If free light chains are unmeasurable, PR is defined as a 50% or greater reduction in (cancerous) bone marrow plasma cells, provided that the baseline percentage was 30% or more. If a soft tissue plasmacytoma (extramedullary tumour) was present at baseline, a 50% or greater reduction in its size is also required.

MR (Minimal Response): A reduction between 25-49% (inclusive) of serum M-protein and reduction in 24-hour urine M-protein by 50–89%. In addition to these criteria, if present at baseline, a reduction of 50% or greater in the size of the soft tissue plasmacytomas (extramedullary tumours) is also required.

SD (Stable Disease): Not meeting the criteria for CR, VGPR, PR, MR, or progressive disease. SD is not recommended for use as an indicator of response, as the stability of disease is best described by estimating the time-to-progression.

PD (Progressive Disease): Requires a 25% increase of one or more of the following:
- Serum M-protein
- Urine M-protein
- If serum and urine M-protein levels are unmeasurable, the difference between involved and uninvolved FLC levels
- If free light chains are unmeasurable, bone marrow plasma-cell percentage
- Development of a new lesion(s)
- If this is the only measure of disease, an increase of circulating plasma cells

Minimal residual disease

Minimal residual disease (MRD) refers to the residual myeloma cells that remain in the bone marrow after treatment. Residual myeloma cells are present at such low levels that they cannot be detected by traditional blood or bone marrow testing.

MRD testing is potentially a very important measurement to detect residual myeloma cells and determine exactly how well treatment has worked. More research on more sensitive and standardized MRD tests is needed before MRD can become a routine clinical measurement.



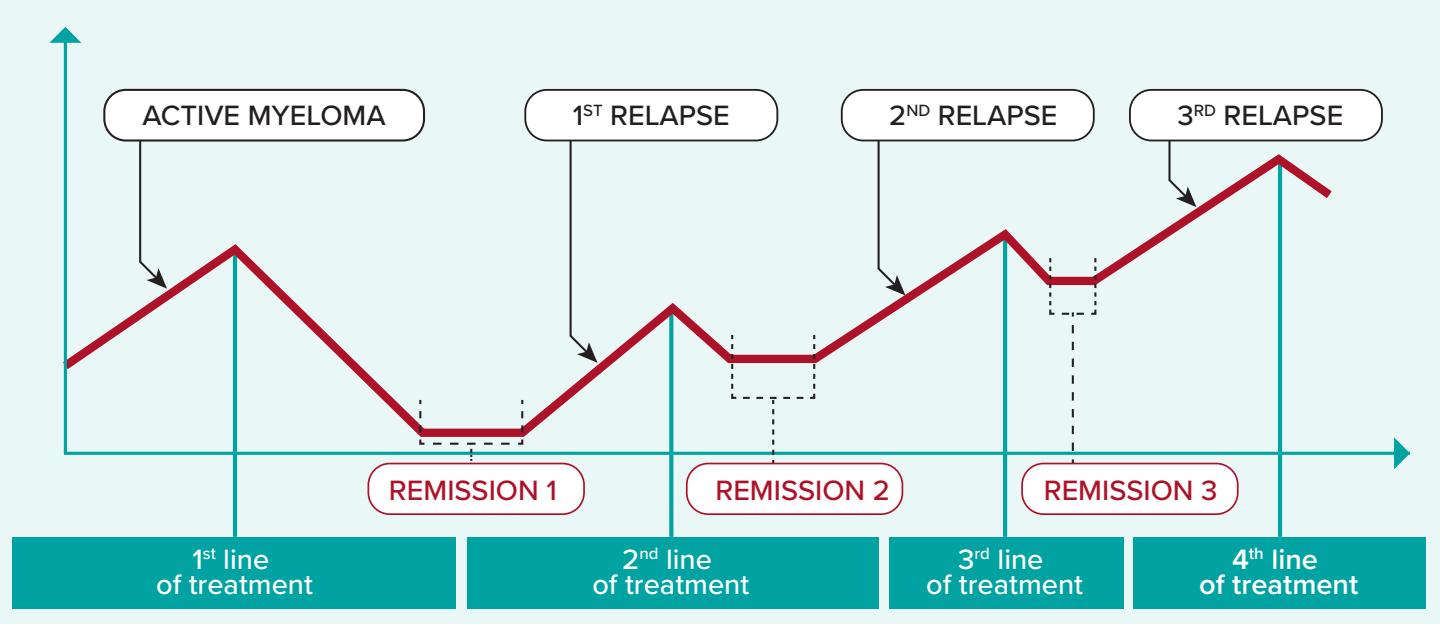


Myeloma relapse

Understanding relapse

Since relapse is common in myeloma, you and your healthcare team must think about your immediate needs, as well as how to keep your future treatment options as open as possible. Treatments are able to kill most myeloma cells, but they're not able to kill them all. With time, residual myeloma cells can start multiplying and lead to relapse.

Figure 2: Understanding relapse



Although the cure for myeloma has not yet been found, novel therapies are enabling individuals to undergo extended periods of remission. Once relapse occurs, treatment options may include:

- a myeloma drug, usually in combination with a steroid such as dexamethasone
- a second transplant
- new treatments through clinical trials

Coping with relapse

Experiencing a relapse in your multiple myeloma can be very stressful. While you may have lived with multiple myeloma for some time, relapse and disease progression can be emotionally devastating. You may experience feelings of distress or fear, mixed with hope, as you navigate this stage of the disease, while also exploring new treatment options for now and the future.

Myeloma Canada's Mental Well-being and Relapse: A resource guide for people living with myeloma on myeloma.ca is a helpful resource to support your mental health and help you determine how wellness strategies fit into your overall cancer treatment plan.

More information

The three Rs of treatment response

Remission: Complete or partial disappearance of the signs and symptoms

Relapse: Reappearance of signs and symptoms of myeloma after a period of improvement

Refractory: Relapse with lack of response to treatment





Overview of myeloma treatments

Observation

Sometimes, the best treatment is no treatment at all. If your myeloma is stable (that is to say, is not progressing or getting worse), a reasonable option may be to simply monitor your condition.

Radiotherapy

High-energy radiation may be used to damage myeloma cells and prevent them from growing. Radiotherapy is typically used on specific parts of the body to treat bone pain and plasmacytomas (tumours in the bone or soft tissue), usually in combination with some form of chemotherapy.

Corticosteroids

Corticosteroids (or steroids) are chemicals naturally produced by the adrenal gland to help prevent inflammation. The synthetic or man-made steroids most commonly used to treat myeloma are prednisone and dexamethasone. Steroids are usually used in combination with other myeloma drugs.

Chemotherapy

Chemotherapy can reduce the number of myeloma cells in the bone marrow. It does not cure myeloma, but it may stop it from progressing or getting worse for a period of time. Cyclophosphamide and melphalan are the two most common chemotherapy drugs still used to treat myeloma in Canada.

Chemotherapy is not specifically "targeted" at myeloma cells, it can also damage healthy cells. It destroys cells that divide rapidly (e.g., cancer, hair, skin, blood, intestines) and can lead to side effects such as nausea, loss of appetite, hair loss, mouth sores, diarrhea or constipation, stomach pain, low blood cell counts, and fatigue.

More information

Central lines

When you are receiving intravenous treatments, you may be given a central line or catheter. You may hear it referred to as a Port-a-Cath, PICC line or Hickman line. A central line is a long, hollow tube made from silicone rubber. It is inserted or tunnelled under the skin of your chest and into a vein. The line can be left in for weeks or months and makes it possible for you to have your treatment without having to have needles inserted at each visit. When it is time for your treatment, the nurse or doctor connects the line to a syringe or intravenous drip. When you no longer need intravenous treatments, the line may be removed.

Stem cell transplantation

Stem cells are a class of cells that are able to divide and develop into specialized cell types. They are normally found in the bone marrow and in the blood and can be used to "repopulate" the bone marrow after receiving high-dose chemotherapy. There are several types of stem cell transplantation approaches that may be used to treat myeloma:

- **High-dose therapy and autologous stem cell transplantation (ASCT)** uses your own stem cells, so you are your own donor. The drug used for high-dose therapy is melphalan (chemotherapy). A second ASCT after relapse may be considered if the first ASCT resulted in a significant benefit (e.g., remission longer than 24-36 months).
- **Allogeneic SCT** involves collecting stem cells from someone else, usually a brother or sister. The donor's cells must match the recipient's tissue type. This approach is not standard practice in myeloma and is generally only done under the supervision of a clinical trial setting.
- A **syngeneic SCT** refers to a transplant using stem cells taken from an identical twin. This is a rare situation but if applicable could be an effective treatment option.
- A **matched unrelated donor (MUD) SCT** refers to a transplant using stem cells taken from a donor who is not a relative but has the same tissue type. This approach is not standard practice in myeloma and is generally only done under the supervision of a clinical trial setting.
- **Tandem (double) ASCTs** are performed in some centres. For a tandem transplant, the plan is to conduct a second transplant within six months of the first one.
- An experimental approach is **ASCT followed by an allogeneic SCT**. With this approach, a patient first undergoes high-dose therapy to reduce the overall number of myeloma cells, followed by an autologous transplant. Next there is a second course of moderately high-dose therapy and an allogeneic transplant of donor stem cells. This would currently only be done as part of a clinical trial.

For more information about stem cell transplant, please refer to Myeloma Canada's High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide on myeloma.ca

More information

Is there an age cut-off for high-dose therapy?

Many myeloma centres have a general rule that high-dose therapy is not routinely offered to people above a certain age, such as 70 or 72 years. These are not hard-and-fast rules. The important thing is not your chronological age but rather your biological age – how generally healthy you are. An otherwise healthy 73-year-old may be a good candidate for high-dose therapy, whereas a 66-year-old with multiple health problems may be a poor candidate.

Immunomodulatory agents (IMiDs)

Immunomodulatory agents work against myeloma by:

- directly attacking myeloma cells;
- stimulating or enhancing the effects of immune system cells that identify and fight myeloma cells.

There are three immunomodulatory agents available for the treatment of myeloma in Canada: thalidomide (e.g., Thalomid), lenalidomide (e.g., Revlimid) and pomalidomide (e.g., Pomalyst). Thalidomide is no longer used in Canada due to the availability of lenalidomide and pomalidomide.

Proteasome Inhibitors (PIs)

PIs block activity of the proteasome in myeloma cells; this is a mechanism that breaks down proteins that are important for controlling cell division. Blocking the proteasome causes proteins inside myeloma cells to build-up to toxic levels, leading to myeloma cell death.

In Canada, there are two PIs available for use in myeloma: bortezomib (e.g., Velcade) and carfilzomib (Kyprolis).

Selective inhibitors of nuclear export (SINE)

SINE drugs block the action of protein called exportin 1 (XPO1) in the nucleus (centre) of myeloma cells. XPO1 is:

- present in high levels in myeloma cells compared to healthy plasma cells;
- important for myeloma cell survival;
- responsible for protecting myeloma cells by moving protein that suppresses tumours to an area inside the cells where they aren't able to reach and kill the myeloma cells.

By blocking XPO1, myeloma cells can undergo a controlled cell death like healthy plasma cells. In Canada, one SINE drug has been approved for the treatment of myeloma: selinexor (Xpovio).

Immunotherapy

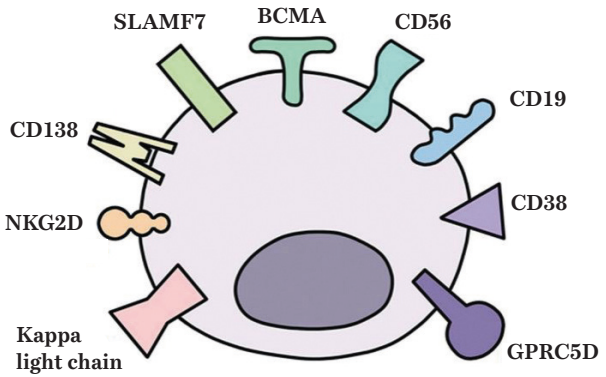
Antigen targets

The goal of immunotherapy treatment is to target antigens that are generally more numerous on the surface of myeloma cells, but not present on most healthy cells. Some antigens may also be on the surface of other cells, so they may not all be possible targets for myeloma immunotherapy.

Several new immunotherapy approaches have been developed to target clusters of differentiation 38 (CD38) and B-cell maturation antigen (BCMA) because they are heavily expressed by nearly all myeloma cells but not by healthy plasma cells. There are also specific antigens on the surface of T-cells that could be helpful to "recruit" other T-cells and enhance myeloma cell destruction.

Figure 3 illustrates some myeloma cell antigen targets that have been studied or are being investigated (at the time of writing), in clinical trials.

Figure 3 – Myeloma cell antigen targets



Monoclonal antibodies (MoAbs)

MoAbs are one of the most significant advances in immunotherapy. They are laboratory-produced antibodies that recognize specific myeloma antigens. MoAbs also recruit several of your immune system cells to destroy myeloma cells. The term "monoclonal" means that there is one type/clone (identical copy) of antibody.

Two MoAbs have been approved for the treatment of myeloma by Health Canada: daratumumab (Darzalex) and isatuximab (Sarclisa). Both drugs target the CD38 antigen. Elotuzumab (Empliciti) targets the SLAMF7 antigen and is also approved by Health Canada but is not sold in Canada.

Chimeric antigen receptor (CAR) T-cell therapy

CAR T-cell therapy is a treatment that is manufactured using T-cells. T-cells are collected from a person's blood by pumping it through a machine that separates the T-cells from the rest of the blood. The collected T-cells are then genetically modified in a lab to express a CAR receptor protein on its surface that can better recognize an antigen on the surface of myeloma cells to kill them more efficiently. Once the CAR T-cells are infused back into the body, they can multiply and continue to exist, allowing for long-term disease control. Unfortunately, after time, CAR T-cells can also stop multiplying and detecting myeloma cells.

As of this writing, two CAR T-cell therapies have been approved for the treatment of myeloma by Health Canada: Idecabtagene vicleucel (Abecma; bb2121) and ciltacabtagene autoleucel (Carvykti; Cilta-cel; JNJ-68284528). Both drugs target the BCMA antigen. Unfortunately, neither of the two approved CAR T-cell therapies are readily available in Canada.

New and emerging therapies being studied in clinical trials

Several new therapies are in development at the time this Handbook was printed. Some of them include:

- Belantamab mafodotin (Blenrep; belamaf;) – an antibody-drug conjugate that targets BCMA
- Elranatamab (PF-06863135) – a bispecific antibody that targets BCMA, as well as CD3 (present on T-cells)
- Iberdomide (CC-220) – a cereblon E3 ligase modulator that targets cereblon
- Mezigdomide (CC-92480) – a cereblon E3 ligase modulator that targets cereblon
- Talquetamab (JNJ-64407564) – a bispecific antibody that targets GPRC5D, as well as CD3 (present on T-cells)
- Teclistamab (Tecvayli) – a bispecific antibody that targets BCMA, as well as CD3 (present on T-cells)
- Venetoclax (Venclexta) – a pro-survival inhibitor that targets Bcl-2, as well as CD3 (present on T-cells)
- Cevostamab (BFCR4350A) – a bispecific antibody that targets FcRH5, as well as CD3 (present on T-cells)
- Modakafusp alfa (TAK-573) – an antibody-cytokine fusion protein (immunocytokine) that targets a different part of the CD38 antigen than daratumumab (Darzalex) and isatuximab (Sarclisa)

For more information about immunotherapy, including new and emerging therapies, please refer to the Myeloma Canada website (www.myeloma.ca) or read Myeloma Canada's Myeloma Immunotherapy InfoGuide.





Treatment options for newly diagnosed patients (First-line therapy)

Clinical trials

Clinical trials are a potential treatment option for newly diagnosed patients. Your medical team may recommend a new procedure, drug, or drug combination that is often not yet approved by Health Canada and therefore unavailable other than through a clinical trial.

Clinical trials may also provide you with access to treatments that are approved by Health Canada but are not covered by your provincial public drug plan. Larger centres will often have multiple clinical trials that can be considered, some funded by pharmaceutical companies and some devised and run by Canadian investigators, such as those of the Canadian Myeloma Research Group (www.cmrg.ca) and the Canadian Cancer Trials Group (www.ctg.queensu.ca). Availability of a clinical trial should always be discussed with your healthcare provider before any therapy is initiated.

Stem cell transplant eligible myeloma

The standard of care and most commonly used therapeutic approach for newly diagnosed transplant-eligible myeloma is ***high-dose therapy and autologous stem cell transplantation (HDT-ASCT).*** Therefore, often the first step is determine your eligibility for the procedure. Your eligibility is evaluated by looking at your overall health, fitness, age, previous treatments and the presence of other diseases or conditions. Please note that it may be possible to defer stem cell transplant (SCT) to a subsequent line of therapy.

People who undergo SCT receive initial (induction) treatment with a combination of the following drugs:

- bortezomib (e.g., Velcade) – a type of proteosome inhibitor (PI)
- dexamethasone – a type of corticosteroid
- cyclophosphamide – a type of chemotherapy
- lenalidomide (e.g., Revlimid) – a type of immunomodulatory agent (IMiD)

The first choice induction treatment combination used in Canada is **RVd:** lenalidomide (oral) + bortezomib (injection) + dexamethasone (oral). Another induction treatment combination that may be used is **CyBord:** cyclophosphamide (oral) + bortezomib (injection) + dexamethasone (oral).

Further along the process, high-dose therapy consists of melphalan (given ***intravenously***). Melphalan is a type of chemotherapy.

Aproximately 60-100 days following the procedure, your medical team may recommend starting daily maintenance therapy with a low-dose of lenalidomide (oral). The goal of maintenance therapy is to prevent disease progression for as long as possible while maintaining a good quality of life. Data from clinical trials has shown that lenalidomide maintenance improves both ***progression-free survival*** and overall survival. Based on the specifics of your diagnosis (e.g., presence of the del17p chromosomal abnormality), your medical team may sometimes recommend maintenance therapy with another drug (e.g., bortezomib). New drugs are being investigated in clinical trials for use as maintenance therapy.

For more information on SCT and eligibility, please refer to Myeloma Canada's High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide on myeloma.ca.

Stem cell transplant ineligible myeloma

If you are not eligible for a stem cell transplant, first-line therapy may involve a combination of the following drugs:

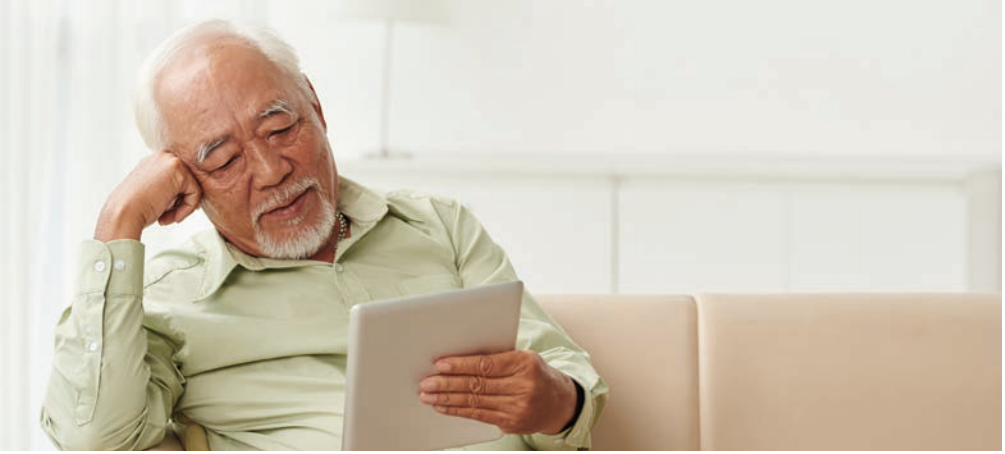
- daratumumab (Darzalex) – a type of monoclonal antibody (MoAb)
- lenalidomide (e.g., Revlimid) – a type of IMiD
- dexamethasone – a type of corticosteroid
- bortezomib (e.g., Velcade) – a type of PI
- cyclophosphamide – a type of chemotherapy
- melphalan – a type chemotherapy
- prednisone – a type of corticosteroid

The first-choice treatment combination in transplant-ineligible myeloma in Canada is:

- **DRd:** daratumumab (injection) + lenalidomide (oral) + dexamethasone (oral)

Other treatment combinations that may be used include:

- **DVMp:** daratumumab (injection) + bortezomib (injection) + melphalan (oral) + prednisone (oral)
- **DCyBord:** daratumumab (injection) + cyclophosphamide (oral) + bortezomib (injection) + dexamethasone (oral)
- **RVd:** lenalidomide (oral) + bortezomib (injection) + dexamethasone (oral)
- **CyBord:** cyclophosphamide (oral) + bortezomib (injection) + dexamethasone (oral)
- **Rd:** lenalidomide (oral) + dexamethasone (oral)





Treatment options at relapse (Second-line therapy and beyond)

The type of second-line therapy that may be offered to you will depend on what first-line therapy you received and if your myeloma responded to the treatment.

For example, if relapse occurs while on lenalidomide maintenance, the myeloma is likely refractory (does not respond) to lenalidomide and the myeloma cannot be re-treated with that drug in subsequent lines of therapy. Furthermore, since lenalidomide belongs to the IMiD drug class, your healthcare team may prefer second-line therapy with a drug (i.e., bortezomib) from a different class (i.e., proteosome inhibitor).

Second-line therapy options

If you received HDT-ASCT as first-line therapy, a second ASCT may be considered after relapse if the first ASCT resulted in a remission longer than 24-36 months. It may also be possible to defer the second transplant to a subsequent line of therapy.

Clinical trials are a potential treatment option for second-line therapy (and beyond) and should always be considered as an option if available. Some new and emerging treatments, including immunotherapy, that may be accessible through a trial include:

- CAR T-cell therapies
- ***Cereblon E3 ligase modulators***
- ***Bispecific antibodies***
- ***Antibody-drug conjugates***
- B-cell lymphoma-2 (BCL-2) inhibitors

Additional second-line therapy options may include a combination of the following drugs:

- daratumumab (Darzalex) – a type of MoAb
- isatuximab (Sarclisa) – a type of MoAb
- bortezomib (e.g., Velcade) – a type PI
- dexamethasone – a type of corticosteroid
- lenalidomide (e.g., Revlimid) – a type of IMiD
- carfilzomib (Kyprolis) – a type of PI
- pomalidomide (e.g., Pomalyst) – a type of IMiD
- selinexor (Xpovio) – a SINE drug
- melphalan – a type chemotherapy
- prednisone – a type of corticosteroid

Treatment combinations that may be used include:

- **DVd:** daratumumab (injection) + bortezomib (injection) + dexamethasone (oral)
- **DRd:** daratumumab (injection) + lenalidomide (oral) + dexamethasone (oral)
- **KRd:** carfilzomib (infusion) + lenalidomide (oral) + dexamethasone (oral)
- **IsaKd:** isatuximab (injection) + carfilzomib (infusion) + dexamethasone (oral)
- **IsaPd:** isatuximab (injection) + pomalidomide (oral) + dexamethasone (oral)
- **SVd:** selinexor (oral) + bortezomib (injection) + dexamethasone (oral)
- **Kd:** carfilzomib (infusion) + dexamethasone (oral)
- **Pd:** pomalidomide (oral) + dexamethasone (oral)
- **Rd:** lenalidomide (oral) + dexamethasone (oral)

Subsequent-line therapy options

Clinical trials are a potential treatment option for subsequent lines of therapy (e.g., third-line, fourth-line, etc.). They may provide access to new and emerging immunotherapy treatments.

Similarly to second-line therapy, treatments that may be available to you at relapse for subsequent lines of therapy (e.g., third-line, fourth-line…) will depend on your previous treatments and how the myeloma responded. Treatment combinations that may be used for subsequent-line therapy include:

- **DVd:** daratumumab (injection) + bortezomib (injection) + dexamethasone (oral)
- **DRd:** daratumumab (injection) + lenalidomide (oral) + dexamethasone (oral)
- **IsaKd:** isatuximab (injection) + carfilzomib (infusion) + dexamethasone (oral)
- **IsaPd:** isatuximab (injection) + pomalidomide (oral) + dexamethasone (oral)
- **SVd:** selinexor (oral) + bortezomib (injection) + dexamethasone (oral)
- **Kd:** carfilzomib (infusion) + dexamethasone (oral)
- **Pd:** pomalidomide (oral) + dexamethasone (oral)
- **Vd:** bortezomib (injection) + dexamethasone (oral)
- **Rd:** lenalidomide (oral) + dexamethasone (oral)





Managing complications and side effects

The build-up of abnormal (myeloma) plasma cells in the bone marrow can cause a number of medical problems. It is important that such problems be identified, monitored and treated.

Bone complications

Healthy bones are continually breaking down (referred to as resorption) so new bone can be laid down. There are two types of cells that are important for healthy bones:

- ***Osteoclasts*** — cells that break down old bone so there is room for new bone to be formed
- ***Osteoblasts*** — cells that follow osteoclasts and strengthen the bone by laying down fresh, new bone

Myeloma cells send signals that speed up the bone breakdown activity of osteoclasts and prevent osteoblasts from making new bone. This vicious cycle of bone loss can lead to:

- areas of damage or "holes" in the bone, known as osteolytic or lytic lesions
- progressive bone thinning, called osteoporosis

When bone thins or there are lytic lesions:

- you may experience bone pain
- you are at increased risk of bone fractures (e.g., rib fracture; compression fracture of the vertebrae in the spine) or breaks

What is done for bone disease in myeloma?

- Imaging tests are routinely performed to detect areas of bone thinning, lytic lesions, and fractures
- People with myeloma are routinely prescribed bone protector drugs that strengthen the bone, such as:
  - ***Bisphosphonates:*** Pamidronate disodium (Aredia), zoledronic acid (Zometa), sodium clodronate (Bonefos)
  - ***RANKL inhibitor:*** Denosumab (Xgeva)
- Radiotherapy (radiation therapy) can be used to treat specific lytic bone lesions and help relieve pain
- Fractures of the vertebrae in the spine have can sometimes be treated by ***vertebroplasty,*** or more lately through ***kyphoplasty***

To learn more about bone complications, read Myeloma Canada's Myeloma Bone Disease InfoGuide.

More information

Is exercise safe?

Unless there are reasons why an individual cannot exercise, mild to moderate exercise such as walking or swimming is usually beneficial for people with myeloma, especially when integrated into their routine on a regular basis. Being active can help you manage side effects from the disease or its treatment. Notably, it may improve your general health and blood circulation, and it can also be physically and emotionally beneficial in reducing pain, insomnia, depression and anxiety. A good exercise regimen also helps prevent health complications, such as thrombosis and peripheral neuropathy.

With myeloma, it is important to avoid contact sports or activities that could result in falls. Make sure that if you're feeling unwell, you take a break and you come back to the exercises later.

Talk to a physical therapist or your healthcare team about activities that would be suitable for you.



Anemia

With myeloma cells crowding the bone marrow, myeloma can result in a reduced red blood cell count. Red blood cells are important because they contain hemoglobin. Hemoglobin carries oxygen from the lungs to the cells of your body, giving you energy and stamina. If hemoglobin is less than 120 g/L in females or less than 140 g/L in males, it is called anemia. Whether anemia requires treatment will depend on its level, how quickly the level is changing, and how well you are feeling and functioning.

Symptoms of anemia include:

- Feeling very tired even though you are getting enough rest
- Looking pale
- Shortness of breath after even mild exertion
- Difficulty with daily chores, concentration or remembering things
- Feeling lightheaded or dizzy

People react differently to having a low hemoglobin count. Some also report headaches, leg pain or feeling cold.

Why treat anemia?

Studies have shown that in people with cancer, treating anemia can help relieve fatigue, make it easier to perform everyday activities, reduce the need for blood transfusions, improve quality of daily life and increase their likelihood of completing cancer therapy.

There are a number of treatment options for anemia, and it is important to discuss all of them with your healthcare team.

- If your anemia is due to a change in your diet, eating healthier or taking iron, vitamin B12 or folic acid (folate) supplements may help. **Always check with your doctor or pharmacist before taking any non-prescription, over-the-counter iron or vitamin supplement, or any herbal remedy.** Some supplements or remedies can interact with prescription medications.
- Blood transfusions can be used to treat severe anemia and can quickly increase hemoglobin levels on a short-term basis.
- Medication that stimulates the body into making more red blood cells can be prescribed. Epoetin alfa (Eprex) and darbepoetin alfa (Aranesp) contain versions of the human hormone ***erythropoietin***, which tells the bone marrow to make more red blood cells. Both drugs are given as an injection just under the skin).

Infections

Myeloma and some of its treatments can affect the normal production of antibodies and reduce white blood cell counts. This can leave a person susceptible to repeated infections or illness, especially respiratory infections, from which it may take a long time to recover.

Annual seasonal flu vaccination is recommended for all myeloma patients. Family members living in the same household as someone with myeloma should also receive an annual seasonal flu vaccine. Live nasal flu vaccines can cause infection in people with myeloma and are not recommended. Furthermore, family members living in the same household should also refrain from taking a live nasal flu vaccine or a live oral vaccine against polio infection.

Pneumococcal vaccination (i.e., Pneumovax) every 5 years is recommended to help prevent infection caused by S. pneumoniae bacteria. In people with myeloma, vaccination with the pneumococcal conjugate vaccine (i.e., Prevnar 13) has been shown to be more effective in preventing infection than the pneumococcal polysaccharide vaccine (PPSV23).

Vaccination to help prevent shingles infection (painful blistering rash) caused by the varicella zoster virus (VZV) is recommended with an inactivated VZV vaccine (i.e., Shingrix). Vaccination with a live shingles vaccine (i.e., Zostavax) is not recommended.

Although COVID-19 levels of infection in the community have dropped to lower levels, people with myeloma remain at risk of serious infection. If you have myeloma, it is still recommended to mask while indoors (especially when in crowded situations) and to follow your healthcare providers' vaccination recommendations for immunosuppressed individuals. If COVID-19 infection is contracted, it is recommended to inform public health and your primary care provider so that treatment can be considered. Lastly, it is important to stay informed about any new variants of concern and follow the guidance of your healthcare team.

Many infections cannot be prevented, so it is important that they be treated as soon as they develop. Fever or other signs of infection or disease should be reported promptly to your healthcare team. Antibiotics may be required.

It is important to have a complete dental examination before you begin any treatment. Because people with myeloma have an increased risk of infection, you may require antibiotics before having any dental work.

More information

Reduce your risk

To reduce the risk of infections and illnesses, remember to practice good hand-washing techniques. When in public places, wash your hands frequently or use a hand sanitizer. Try to avoid situations where you may come into contact with people who are ill, or consider wearing a protective face mask.

Kidney damage

M-protein produced by myeloma cells are cleared from the body by the kidneys. Over time, the elevated levels of M-protein in the blood and urine can damage the kidneys. This is why renal function is assessed regularly through routine blood tests. The best way of preventing kidney damage (renal disease) is to treat the myeloma and keep M-protein levels as low as possible. Sometimes – but infrequently – if renal dysfunction is severe, ***dialysis*** may be required.

For more information, please refer to our Myeloma and the Kidney InfoGuide on myeloma.ca.

More information

Drink up!

Drinking lots of fluids can help flush medications and toxins from your body, maintain normal blood volume and pressure, lubricate joints, limit fatigue, and help prevent kidney damage. The best single fluid to drink is water. Unless you are advised otherwise by your healthcare team, try to gradually increase your intake until you are drinking 6-8 glasses of water every day.

Try to limit drinks that contain caffeine, such as coffee, tea and soft drinks. Caffeine and alcohol increase your urine output and can lead to dehydration and fatigue.

Elevated blood calcium (hypercalcemia)

Your bones are constantly being broken down and rebuilt. When old or damaged bone is broken down, the calcium in the bone is released into the bloodstream. Myeloma commonly causes excess bone breakdown that can cause hypercalcemia. Symptoms can include constipation, increased frequency of urination, weakness and in extreme cases, confusion.

Hypercalcemia is treatable and can be prevented or resolved with bone protectors (e.g., bisphosphonates; RANK inhibitors). These drugs help prevent bone breakdown and limit the amount of calcium released from the bones and into the bloodstream.

More information

Hold off taking calcium supplements

In people without myeloma, calcium supplements are often recommended for bone health. But if you have myeloma, never take a calcium supplement without checking with your doctor. Severe hypercalcemia is a medical emergency that requires prompt treatment.

Other blood complications

Myeloma can result in other complications of the blood, although most are relatively rare. If the number of platelets in the blood drops below a healthy level, normal clotting will be affected. This can lead to bruising or excessive bleeding.

When combined with steroids, some medications, such as lenalidomide (e.g., Revlimid) and pomalidomide (e.g., Pomalyst) can also increase the risk of blood clots in the veins, such as those in the legs – known as deep vein thrombosis (DVT) – a potentially dangerous complication. Blood-thinning medications can be prescribed to reduce the risk of blood clots.

In a small number of people, a high M-protein level can cause the blood to thicken (known as hyperviscosity) and decrease blood flow to the skin, fingers, toes, nose, kidneys and brain.

Pain and fatigue

Pain in myeloma can be due to the effects of the myeloma itself, side effects related to treatment, as well as medical tests or procedures. The most common causes of pain in someone with myeloma are usually due to weakened or fractured bones, peripheral neuropathy, plasmacytoma, and infection. Each may cause different degrees of pain. Pain can also be a sign of other disease and

treatment-related side effects or even disease progression. It's very important to discuss any new or persistent pain with your healthcare team as quickly as possible.



Peripheral neuropathy

Peripheral neuropathy is a type of pain that may be experienced as numbness, tingling, increased or decreased sensitivity or pain in your body's extremities (i.e., hands, feet, arms or legs). The symptoms of peripheral neuropathy can vary and will depend on which nerves are affected – the hands and feet are the areas most commonly affected in myeloma. The symptoms often start out mild but can increase and become more serious over time. They tend to travel up the arms and legs. If you develop any new pain or sensation, speak to your doctor or nurse immediately.

Fatigue

Fatigue related to myeloma is not fully understood, however it can be one of the most debilitating symptoms that may affect you physically, psychologically and emotionally. Fatigue is different than just feeling tired. It's described as a persistent sense of tiredness that isn't proportional to recent activity or that takes longer than expected to go away – even with extra sleep. In severe cases, you may feel too tired to eat, think or even move. Small amounts of activity can be exhausting, and your daily routine, work and social life can become disrupted. You may find that your fatigue increases initially when you start treatment, but once you've been through a few treatment cycles and your myeloma is under control, your fatigue may improve. Like so much else, fatigue is experienced differently by everyone and may vary in its severity: it may be mild or it may be so severe that it substantially reduces your quality of life.

For more information on pain and fatigue in myeloma and types of medication used to treat, improve or reduce these conditions, please refer to Myeloma Canada's Managing Pain & Fatigue InfoGuide on myeloma.ca.

More information

Alternative therapies

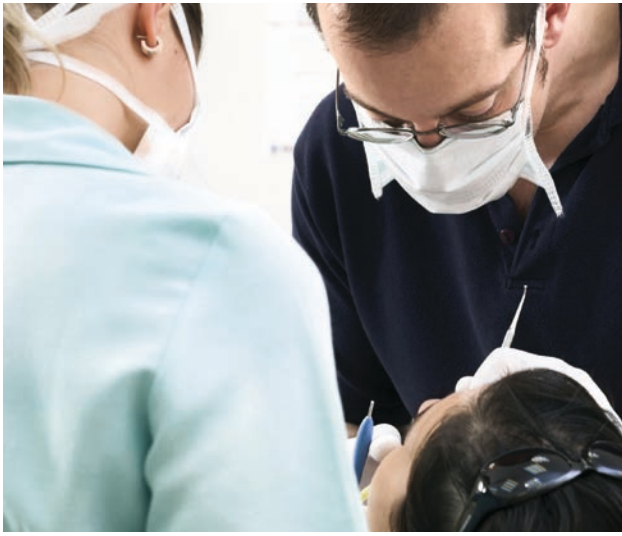
Many vitamins, supplements and herbal therapies can interact with your cancer medications. Before taking any vitamin, supplement or herbal therapy, talk to your physician and/or your pharmacist.

Osteonecrosis of the jaw (ONJ)

ONJ, or abnormal death (necrosis) of the jaw bone, is a relatively rare side-effect of long-term bone protector drugs (see page 27 for more information). The risk of ONJ appears to be higher among those taking zoledronic acid compared to pamidronate. It can occur spontaneously but appears to be more likely following particularly traumatic dental work such as extractions. Before starting bone protector therapy it is recommended that you:

- check if your cancer centre has a dental clinic
- have a complete dental examination
- arrange to have any oral surgery or tooth extractions done

Restorative work such as fillings, bridges, crowns and root canals are likely safe, provided that the wounds are as small as possible and all the rough edges are carefully smoothened. Ask your dentist to speak with your doctor about any other special precautions you may require, especially when receiving treatment.



Once you've started taking bone protectors, it is recommended that you:
- Practice good oral hygiene to reduce the odds of needing dental care
- Visit your dentist regularly to catch problems when they are small
- Avoid extractions and peridontal surgery if possible
- Do not have dental implants
- Take all of your medications as prescribed
- Drink lots of water – at least 6 to 8 glasses a day
- Keep your doctor informed on your dental health
- Report any side effects to your doctor as quickly as possible

Chemotherapy side effects

All prescription medications have intended effects (treatment) and others that you may not want, commonly known as side effects. Your healthcare team, particularly your pharmacist and nurse educator, can explain what side effects you can expect from the medications you are prescribed, which ones to report right away, and what can be done to relieve them.

Common side effects of chemotherapy are:
- **Nausea and vomiting —** Anti-nausea (anti-emetic) drugs can help to prevent and control nausea and vomiting. Avoiding strong smells and getting lots of fresh air may also help. Vomiting can dehydrate you, so it is important to try and keep taking sips of cool drinks.
- **Hair loss (alopecia) —** Hair loss is common with some kinds of chemotherapy, such as melphalan (Alkeran®), but not all. If it occurs, remember that your hair will grow back once your treatment has finished.
- **Changes in the mouth —** Depending on the type of chemotherapy you are receiving, you may experience mouth sores, or a sore or dry mouth. Medicines or a special mouthwash can help prevent or treat mouth ulcers. When undergoing high-dose therapy (e.g., melphalan), sucking on ice chips may also help ward off mouth sores. Keep your teeth clean by regularly using a soft toothbrush, and try to avoid things that might irritate your mouth such as spicy, salty or tangy foods. If you have a sore or dry mouth, avoid foods that stick to the roof of your mouth (e.g., peanut butter or chocolate) and mouthwashes that contain alcohol. Moisten your food with gravy or sauces and try drinking through a straw or sucking ice cubes or frozen treats.
- **Loss of appetite —** At times over the course of your treatment, you may have no appetite or feel you cannot face food. To avoid losing weight, try to eat small amounts of food – particularly fresh fruits and vegetables – frequently throughout the day. Or if you feel hungry at some parts of the day and not at others, eat your larger meal when you are hungry. No matter what you eat, be sure to always drink plenty of fluids.

Corticosteroids (steroids) side effects

Corticosteroids (steroids) such as dexamethasone are frequently used to treat myeloma. Side effects can include:
- Fluid retention and swelling, particularly if you also have congestive heart failure
- An increase in blood sugar, which is of concern to people with diabetes or at risk of diabetes
- Insomnia
- Increased appetite
- Indigestion or heartburn – speak to your physician about medication to prevent this problem
- Hiccups
- Blurred vision – it may be short-term (acute) or long-term if due to cataracts
- Mood or emotional changes, such as depression, mood swings, agitation, anxiety, or even psychosis

Other side effects that can develop after long-term use of high-dose steroids include the Cushingoid appearance (weight gain with a "moon face"), osteoporosis or bone loss, and muscle weakness and/or wasting. Fatigue and depression are other potential side effects.

More information

Coping with "'Roid Rage"

Dealing with the diagnosis of cancer is hard – for you and your loved ones. The mood changes brought about by steroids can add to that burden. It is important that you talk to your loved ones and explain the effects steroids can have on your mood and activity levels. Give them a "heads up" when you will be going on and off your medication. Family members and friends can help by being supportive and understanding that sometimes "it's the 'roids talking".

Pain killer side effects

Pain killers can cause side effects that include (but are not limited to):

- Nausea, vomiting, diarrhea or constipation
- Drowsiness, confusion (discuss whether it is safe to drive with your healthcare provider)
- Dyspnea, pulmonary edema, wheezing, coughing
- Peripheral edema, hypertension, chest pain
- Hyperglycemia
- Headache, dizziness
- Muscle spasms
- Insomnia, anxiety
- and more

Ask your healthcare team for medical advice before taking any medication.

Depression

Some studies suggest that up to 40% of cancer patients experience depression or anxiety. As you deal with your disease, periods of feeling "blue" or "down" are not unusual. After all, you are going through a lot of changes. You may sometimes feel that you are no longer the person you used to be. Physical and mental changes may threaten your sense of self-worth and self-esteem.

If depression lasts for many weeks without relief or is severe enough that it interferes with everyday life, you may need some help. Talk about your feelings with your doctor, nurse or a mental health professional. Sometimes just talking with someone is enough to help. In other cases, medication can be prescribed to help relieve depression.



Speak to a healthcare professional if you experience five or more of the following symptoms for more than two weeks:

- Feeling sad, anxious, irritable, nervous and/or guilty
- Feelings of worthlessness or hopelessness
- Changes in your usual sleep patterns (either having trouble sleeping or sleeping more than usual)
- Changes in your appetite; gaining or losing weight without trying
- Loss of interest in activities you used to enjoy
- Restless or slowed behaviour
- Persistent or recurring headaches, digestive disorders, or ***chronic*** pain
- Difficulty concentrating, remembering or making decisions
- Fatigue, loss of energy
- Change in work style or productivity
- **Thoughts of suicide – if these occur, seek immediate professional help**

Please refer to Myeloma Canada's Mental Well-being and Relapse: A resource guide for people living with myeloma at myeloma.ca for more information.





Your healthcare team

When you were diagnosed with myeloma, you may have felt like you were alone in the battle of your life. But in reality, there is a whole team of dedicated professionals who are behind you and ready to help: they are the members of your healthcare team. In this section, we'll begin by looking at each of their roles. Then we'll discuss how you can optimize communication with your team members to become a more informed and active participant in your care.

Family doctor

When you became ill, the first person you probably saw was your family doctor. Your family doctor helped narrow down the possibilities of what might be wrong and provided you with referrals to specialists. Most family doctors see only a few, if any, people with myeloma in their practices.

Hematologist or oncologist

Because myeloma is a cancer of the blood, you may be referred to a hematologist, a physician who studies, diagnoses and treats diseases and disorders of the blood. Some hematologists specialize in blood cancers, whereas others may concentrate on other blood problems such as clotting disorders. A hematologist or oncologist is often the key member of your healthcare team when you have myeloma. In some cases, myeloma is diagnosed, followed, and managed by a medical oncologist – a physician who specializes in the diagnosis and treatment of cancer.

Nurse practitioner

A nurse practitioner is a nurse who has undergone advanced training and has the authority, under specific circumstances, to diagnosis and treat patients. This can include prescribing certain medications. In some areas, a primary care practice may be led by a nurse practitioner.

Radiation oncologist

If you require radiotherapy, you will be referred to a radiation oncologist. As the name implies, a radiation oncologist is a physician who specializes in treating cancer with radiotherapy.

Surgical oncologist

A surgical oncologist is a surgeon who specializes in cancer operations. For example, if a plasmacytoma must be removed, you may be referred to a surgical oncologist.

Nurse

Nurses are key members of of your healthcare team and may fill several important roles. An oncology nurse is a specially-trained nurse who works closely with your hematologist and radiation oncologist to coordinate your care, oversee your therapy and keep your physicians informed of any problems you may encounter. Other nurses may specialize as cancer educators. Nurses are invaluable sources of information and support.

Orthopedic surgeon
If you require surgery on your bones, muscle or joints, you may be referred to an orthopedic surgeon.

Pharmacist
Your treatment for myeloma will involve many medications, some of which may be oral and others which may be delivered through an intravenous line. Whether working in the hospital or the community, pharmacists are valuable sources of information for patients and care providers. Pharmacists can help you understand what different medications are designed to do, how to take them, what effects and side effects to expect, and what to do if side effects occur.

Dentist
Your dentist is an important but often overlooked member of your healthcare team. Good oral health is important at all times, and even more so when you are undergoing myeloma treatment. Infections from the teeth can drain into the lymph glands in the neck, and if your teeth and gums are not kept clean, large quantities and varieties of bacteria can colonize the gums. These types of infections are an important and preventable source of problems.

If possible, it is best to identify and treat dental problems before you start chemotherapy, undergo stem cell transplant, or start taking bisphosphonates. Generally, the best time to be treated is when your hemoglobin count is 100 g/L or more, platelet count is 80 x 10^9/L or more, and your absolute neutrophil count is adequate. Special precautions such as prophylactic antibiotics may or may not be required if you have a central line or catheter in place.

Dentists who work at cancer centres are familiar with the special requirements that people with myeloma have, some community dentists may not be. Speak to your dentist and clearly outline what drugs you are taking (including intravenous therapies), where you are in your therapy and what the plans may be for the future. You should especially mention that there may be jaw related problems if you are taking a bisphosphonate. Encourage him or her to talk to a cancer centre specialist.

Registered dietitian/nutritionist
Cancer and cancer treatment can make eating difficult. You may find it difficult to eat enough – or to eat the right kinds of food – to keep your strength up. Or some medications can increase your appetite, making it difficult to avoid overeating. A dietitian can help you maintain the healthiest diet possible throughout the different stages of your treatment. If you are struggling with nausea, vomiting, anorexia (loss of appetite) or a dry or sore mouth, your dietitian can suggest foods or drinks to help.

Psychiatrist or psychologist
A psychiatrist is a physician trained in the diagnosis and management of mental health. A psychologist is not a physician, but someone who has advanced training in counselling and human psychology. Both psychiatrists and psychologists can be very helpful in dealing with the psychological, emotional or behavioural problems you may encounter. In addition to “talk therapy”, psychiatrists are licensed to prescribe medication, such as anti-depressants, if required.

Social worker or counsellor
Like a psychologist, a social worker or counsellor can help you deal with the many psychological, emotional, and/or behavioral challenges a myeloma diagnosis can cause. In addition, a social worker may be able to help you deal with some of the practical issues that arise, such as finding out more about your healthcare coverage, and other resources.

Clergy or spiritual advisor
Some people find that talking with their clergy or spiritual advisor can be very helpful.








Optimizing communication

As you probably know only too well, most healthcare professionals are very busy. Their time to talk is often limited. And most healthcare professionals are so used to the medical terms they use that they may forget that other people do not understand them. Here are some tips for optimizing communication with your healthcare team.

- Write down any questions you have as well as any side-effects or symptoms you are experiencing. Bring these lists or documents with you to your appointment. Give the list to your doctor at the beginning of your consultation. Don't wait until the end, when the doctor is out of time.
- Bring a notepad or laptop to take notes during your consultation of what your doctor says. If you can, it's best to bring someone with you to take notes for you. Some people find it helpful to tape their appointments on their phones or devices so that they can easily refer back to what was discussed. It's best to mention this to your healthcare professional at the beginning of your appointment.
- Ask your doctor if he or she has an assistant or nurse that you can talk to whenever you have questions.
- Ask if there are any brochures or other educational material you can take home with you. Gathering documentation in a binder to keep the information all together is also a good idea.
- Keep your own records of your medical history and treatment. Many people find it helpful to keep a binder or file in which they write down their appointments and treatments, who treated them, what medications they received, and their test results. In Canada, patients by law must be given access to their medical information if they request it (a reasonable fee may be charged to cover administrative costs). Creating and maintaining your own binder of information will give you a better understanding of your condition, and may be helpful when dealing with healthcare professionals who are not familiar with your condition.

Not certain of what to ask?

Below are some sample questions for different members of your healthcare team.

For your **hematologist, oncologist** or **radiation oncologist:**

- What are the results of my tests and what do they mean?
- What are all my treatment options, which one do you recommend and why do you feel this is the best approach?
- Are there clinical trials available at this centre or other centres that I could consider? If they are uncertain, ask them to please contact a referral centre to inquire.

For your **surgical oncologist** or **orthopedic surgeon:**

- Can you explain my surgical procedure in detail?
- What should I expect before, during and after surgery? What will my recovery be like?

For your **oncology nurse** or **educator:**

- What is your role in my cancer care? Who should I contact if I have problems, especially after hours or on weekends? Ask for names and telephone numbers.
- What activities can you suggest so I can stay as active as possible? Which activities should I avoid?

For your **pharmacist:**

- What is the purpose of this medication? What side effects are likely to occur and which ones should I report immediately?
- Can you help me set up a system, such as daily pill boxes or blister packs, to ensure I take all of my medications as prescribed?

For your **dentist:**

- Are you familiar with the requirements for treating someone with myeloma and/or with a central line in place?
- What can I do to reduce the risk of requiring extractions or other traumatic dental work while undergoing treatment?

For your **dietitian:**

- I'm finding it difficult to eat. Is there anything you can recommend to help me?
- I'm going to start a new therapy soon. What do we know about this treatment's effect on appetite, digestion, etc.? Is there anything you can recommend to reduce its effects?

F

or your **psychiatrist, psychologist, counsellor** or **spiritual advisor:**

- Can you help me better deal with the emotional effects of my diagnosis?
- My family and loved ones are very upset about my illness. What can I do to help them?

For your **social worker:**

- Can you help me and my family to learn ways of coping with the changes brought by my disease?
- Can you help me figure out what healthcare or other benefits I may be eligible for, such as short or long-term disability leaves?

More information

As a patient, you have rights and responsibilities when interacting with the members of your healthcare team.

Rights:

- To be treated with respect and courtesy
- To be your own advocate or to bring an advocate with you
- To be kept fully informed and to have things explained to you in language you can understand
- To be informed of all possible treatment options available at your centre or other facilities, including, and especially, clinical trials
- To be allowed, and helped, to obtain a second opinion if you want one
- To be given the opportunity to participate in treatment decision-making, including the right to refuse any treatment you do not want
- When you ask, to receive copies of your records, such as lab results, X-rays, and test results, at a reasonable cost (e.g., administrative cost)

Responsibilities:

- To tell the whole truth and nothing but the truth
- To speak up if you aren't happy or don't understand (it helps to be tactful when doing so)
- To try and learn about your condition and treatments so you can participate in decisions regarding your myeloma journey
- To comply with any mutually acceptable treatment plan
- To treat the members of your healthcare team with respect and courtesy

To learn more about advocacy and your rights, please refer to Myeloma Canada's Advocacy Handbook on myeloma.ca.





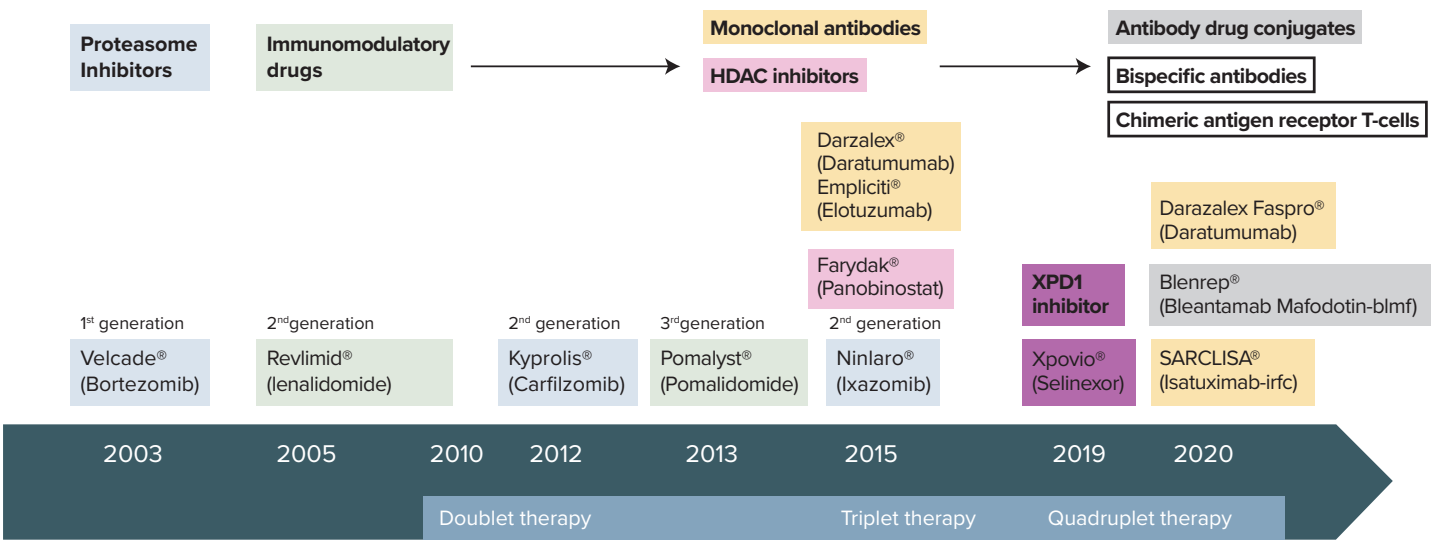
Development, approval and reimbursement of new and emerging therapies

For decades, only a very small number of therapies were available for myeloma. Today, the treatment of myeloma has entered a new and exciting phase. Research into the underlying cellular and biochemical processes of the disease is making a variety of innovative therapies possible. In this section, we'll look at how new therapies are developed and the approval process they must undergo. We'll also look at how new therapies are paid for.

History of myeloma research

Over the past 20 years, the development of new therapies has resulted in treatment combinations that have improved the quality of life and extended the lives of many people with myeloma (Figure 4).

Figure 4: Development timeline of classes of myeloma therapies



Adapted from Nishida H. Cancer (Basel). 2021;13(11):2712. doi: 10,3390/cancers13112712
Note: Corticosteroids (i.e., dexamethasone, prednisone) are omitted from the figure above.

Development of new therapies

Developing new therapies is a long and very expensive process. A number of phases or types of studies are required.

1. Pre-clinical research

The research that eventually leads to new drugs or treatments typically begins in a laboratory. Using study results of the basic genetic, cellular or biochemical processes that can lead to myeloma, scientists test different molecules or substances. This research may begin by using cells in a test tube (in vitro) and if promising, proceed to testing in small animals such as rats or mice (in vivo). Repeated animal trials are required to establish that a new agent is safe before it can be tested in any humans. Many molecules may be studied, but only the most promising will make the leap from pre-clinical to clinical trials.

2. Clinical trials

Clinical trials are research studies that involve people, therefore all clinical trials must be: 1) reviewed by Health Canada; 2) shown to be safe; and 3) approved by Ethics Committees of all the participating hospitals. These rigorous review processes are in place to protect the safety of participants and only studies that are approved are allowed to recruit patients.

More information

Clinical trials are divided into various steps called phases. As described by the Canadian Cancer Society, here are the most common phases of clinical trials:

- **Phase I trials –** this is often the first time a new therapy is tested in people. This phase is used to see how safe a treatment is and establish the best dosage. Phase I trials are often offered to people with advanced cancer, or who are no longer responding to treatment, or who have no other treatment options. There are usually 15 to 30 people in a Phase I trial.
- **Phase II trials –** the focus is on how well a treatment works. Throughout this phase, the safety of the treatment and its possible side effects are carefully studied. There are usually fewer than 100 people in a Phase II trial.
- **Phase III trials –** here, a promising new treatment is compared to the standard (or commonly used or accepted) treatment for a condition or a disease. The intent is to discover if the new treatment is better than the standard one being used. Phase III trials may include people from all over the world and may have anywhere from several hundred to several thousand participants.
- **Phase IV trials –** more information is gathered on possible positive and negative effects of the new treatment once it has been approved for use. There are usually several hundred to several thousand participants in this phase.

We recommend you visit the Canadian Myeloma Research Group website to become familiar with drug development and database work being done in Canada (www.cmrg.ca).

Myeloma research in Canada

Canadian Myeloma Research Group (CMRG)

CMRG is the only organization dedicated solely to myeloma research in Canada. They are made up of over 50 researchers across 30 research centres and are recognized as a global leader in myeloma research. CMRG has three core research platforms:

1. **Clinical trials:** CMRG helps bring cutting edge laboratory discoveries into clinical trials quickly and efficiently for Canadian patients. They work in collaboration with pharmaceutical companies, network members, and patients to facilitate cost effective trials that can recruit participants quickly. They strive to conduct trials that deal with drugs, and drug combinations, that are most effective for the treatment of myeloma while minimizing side-effects.
2. **Real-world evidence:** CMRG has one of the largest and most comprehensive multiple myeloma databases in the world. Real time patient data is collected on an ongoing basis from multiple centres across the country. This research provides evidence-based information to:
   - optimize treatment options for people living with myeloma and drive better decisions in the healthcare system to catalyze new myeloma treatments
   - identify gaps to catalyze new treatments
   - provide insight into regional differences
   - inform healthcare policy decisions

3. **Translational research:** CMRG recognizes the importance of laboratory research to better understand myeloma biology. They work with multiple centres across Canada to perform dynamic translational research. Their long-term goal is to create a National Biobank of bio-specimens (blood and bone marrow) to:
   - develop a streamlined platform for sample acquisition, transport, and storage
   - direct advancement of myeloma research by linking clinical outcomes with laboratory discoveries

Learn more at www.cmrg.ca.

Canadian Cancer Trials Group (CCTG)

CCTG is an academic cooperative oncology group that designs and conducts clinical trials testing cancer therapy, supportive care and prevention interventions across Canada. The Group is a collaborative network of researchers, physicians, scientists, statisticians and patients internationally recognized for finding the treatments that give people with cancer longer, better quality lives. Learn more at www.ctg.queensu.ca.



You can contribute to myeloma research

As someone with myeloma you may be able to make an invaluable contribution to myeloma research and the development of new therapies. Perhaps you can donate marrow for laboratory research, or volunteer for a clinical trial. Speak to your doctor or your healthcare team.

If you are considering a clinical trial, don't be afraid to ask a lot of questions. The more you know about a study, and all the other options available to you, the more informed your decisions will be. For more information about clinical trials and how they work, refer to Myeloma Canada's Clinical Trials as a Treatment Option InfoGuide. To find clinical trials that are recruiting patients in Canada, please use the Clinical Trial Finder tool or refer to the following websites:

- www.cmrg.ca/research/clinical-trials
  - CMRG is the only organization dedicated solely to myeloma research in Canada. This uniquely positions them to provide infrastructure and expertise in the administration of prospective and retrospective clinical studies across Canada.
- www.clinicaltrials.gov
  - This website is a service provided by the US National Institute of Health.
- www.canadiancancertrials.ca
  - A Canadian website that allows you to search by cancer type and location.
- https://health-products.canada.ca/ctdb-bdec/index-eng.jsp
  - Health Canada's Clinical Trials Database

The drug approval process in Canada

Before a drug can be used in Canada, it must go through a rigorous approval process by Health Canada. Health Canada does not look solely at whether a new agent is safe, but at the balance between risks and benefits.

If the drug company's submission is approved, Health Canada will issue a Notice of Compliance (NOC) and give the drug a Drug Identification Number (DIN). This means the company is now allowed to market the new drug in Canada.

Once a new cancer drug is approved for use in Canada, the manufacturer must make a submission to stakeholders set up by the provincial and territorial Ministers of Health to make recommendations as to whether new drugs should be covered under provincial formularies – the list of medications they will pay for.

If approved, the pan-Canadian Pharmaceutical Alliance (pCPA) will then conduct joint price negotiations with the drug manufacturers on behalf of the federal, provincial and territorial governments for new drugs in Canada.

Despite the national review processes that are in place, most publicly funded drug plans continue to make their own decisions as to which medications they will or will not list. As a result, the coverage of new treatments often varies across the country.

Reimbursement of new therapies

There are basically four ways of paying for cancer drugs:

1. You are a member of a government health insurance drug plan that the medication is approved and listed on (either as a general benefit or through a special authorization process)
2. You have a private drug plan that will pay for the drug (many private plans have formularies or lists of drugs covered)
3. You pay for the drug yourself
4. If you meet certain financial eligibility criteria, assistance may be provided by the drug manufacturer

It may take some research to ensure you have optimal access to new prescription medications – and to minimize your own out-of-pocket costs. To learn more, please read Myeloma Canada's Financial Implications of Living with Myeloma online InfoGuide and ask your oncologist for any information or help they may be able to provide.





How to be your own advocate



Being diagnosed with cancer can be overwhelming as you are facing a number of major life changes. One of the most important things you can do to help yourself is to become your own advocate.

Here are a few tips that can make a difference over the course of your myeloma journey:

- Document your experience
- Ask for a second opinion
- Sort out the information or services you need and identify the appropriate person to address each one
- Prepare for each appointment
- Take, review and store notes of your visits
- Educate yourself
- Involve others
- Find a support group in your area

To help you navigate through your different rights and to learn how to advocate for yourself, for others and for change, please refer to Myeloma Canada's Advocacy Handbook on myeloma.ca.





About Myeloma Canada

Myeloma Canada is a registered non-profit organization created by, and for, people impacted by multiple myeloma. As the only national organization exclusively devoted to the Canadian myeloma community, Myeloma Canada has been making myeloma matter since its founding in 2005.

Working with leading myeloma researchers and clinicians as well as other cancer organizations and local support groups across Canada and internationally, Myeloma Canada seeks to strengthen the voice of the Canadian myeloma community and improve quality of life for those impacted by myeloma through awareness, education, advocacy, fostering an empowered community and supporting clinical research to find a cure.

Myeloma Canada's goals:

- **Increase awareness** of the disease and its effects on the lives of patients and their families
- **Educate** patients, families and caregivers
- **Advocate** for access to new therapies, treatment options and healthcare resources
- **Empower** patients and caregivers through community engagement
- **Advance** clinical research and promote access to new drug trials in Canada

Myeloma Canada educational publications

For more detailed information about myeloma and living with the disease, visit myeloma.ca. From here, you can download Myeloma Canada's educational publications, watch educational videos, find a local support group and so much more.

Whether you're downloading a copy or requesting a printed version, all Myeloma Canada publications are free of charge. To order your printed copies, email us at contact@myeloma.ca, or call us toll-free at 1-888-798-5771.

Myeloma Canada would like to thank AbbVie Inc., Amgen Inc., The Binding Site Group Ltd., Bristol-Myers Squibb Company, GlaxoSmithKline Inc., Janssen Global Services, Pfizer Inc. and Sanofi for providing unrestricted educational grants that partially funded and helped make the creation of this Handbook possible.





Beyond family and friends: Myeloma support groups and programs

Local support groups and programs

Talking to people outside your immediate circle may be easier than talking to family and close friends. Meeting and speaking with others with shared experiences can truly provide you with invaluable information and support. Others may be, or have already been, in a similar situation to yours. They understand what you're going through and how to help from a different perspective. Sometimes relief can be found just by speaking to people that can personally identify and relate to you, your experiences and your feelings.

Visit myeloma.ca to find a support group near you. If a physical support group doesn't exist in your area, consider forming one yourself. Myeloma Canada can help you get started.

Virtual, online support groups

You may also be able to meet and connect with others through an online support group. Myeloma Canada has created, and is the lead administrator of many online, virtual patient support groups on Facebook. These closed groups offer a safe environment to connect and exchange experiences with others facing similar challenges. Thanks to the Facebook "translate" button, language barriers can be overcome, enabling you to communicate, in your mother tongue, with people nation-wide. Moreover, the information shared on the page is private and can't be viewed by the public. All members must request to join the group to gain access.

Myeloma peer support

In addition to joining a support group, you may want to talk with someone who has first-hand experience either living with myeloma, or as a caregiver to someone with the disease. Myeloma Canada's Myeloma Peer Support program provides you with this opportunity.

You are not alone

Visit myeloma.ca to find a support group near you, learn more about our online Facebook support groups, our peer support programs, and other support resources.





Glossary

Albumin: Simple water-soluble protein that is found in the blood.

Amyloid light-chain (AL) amyloidosis: A condition in which myeloma light chains (M-protein) are deposited in tissues and organs throughout the body. This occurs more commonly with lambda (λ) versus kappa (κ) M-protein. In patients with amyloidosis, light chain protein binds to certain tissues such as heart, nerves and kidney rather than being excreted out of the body through the kidneys.

Anemia: A decrease in the normal number of red blood cells typically monitored through the hemoglobin level. Myeloma in the bone marrow blocks red blood cell production, causing shortness of breath, weakness, and tiredness.

Antibodies: Protein that are produced by certain white blood cells (plasma cells) to fight infection and disease in the form of antigens such as bacteria, viruses, toxins or tumours. Each antibody can bind only to a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies disable antigens directly, while others make the antigen more vulnerable to destruction by other white blood cells.

Antibody-drug conjugates: Monoclonal antibodies (MoAbs) attached to a drug.

Antigen: Any foreign substance (such as a bacteria, virus, toxin or tumour) that, when introduced into or arising in the body, causes the immune system to produce natural antibodies.

Aspiration: The process of removing fluid or tissue, or both, from a specific area.

B cells: White blood cells that develop into plasma cells in the bone marrow and are the source of antibodies. Also known as B lymphocytes.

Baseline: Observations or values that represent the initial level of a measure. Values that are taken after a medical intervention are compared to the initial (baseline) values in order to measure the response to treatment.

Basophil: A type of white blood cell. Basophils are granulocytes.

Bence-Jones protein: A myeloma protein present in urine. The amount of Bence-Jones protein is expressed in terms of grams per 24 hours. Normally a very small amount of protein (less than 0.1 grams per 24 hours) can be present in the urine, but this is albumin rather than Bence-Jones protein. The presence of any Bence-Jones protein is abnormal.

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. MGUS is a benign condition.

Beta-2 microglobulin (b2M): A small protein found in the blood. High levels occur in people with active myeloma. Low or normal levels occur in people with early myeloma and/or inactive disease. Approximately 10% of patients have myeloma that does not produce b2M. For these individuals, b2M testing cannot be used to monitor the disease. At the time of relapse, b2M can increase before there is any change in the myeloma protein level. Therefore, 90% of the time, b2M is very useful for determining disease activity.

Biopsy: The removal of a sample of tissue for microscopic examination to aid in diagnosis.

Bispecific antibodies: Laboratory-produced antibodies that target two antigens (one on myeloma cells and one on T-cells to link them together).

Bisphosphonate: A type of drug that binds to the surface of bone where it is being resorbed (or destroyed) and protects against osteoclast activity.

Blood cells: Minute structures produced in the bone marrow; they include red blood cells, white blood cells and platelets.

Bone marrow: The soft, spongy tissue in the centre of bones that produces white blood cells, red blood cells and platelets.

Bone marrow aspiration: The removal, by a needle, of a sample of fluid and cells from the bone marrow for examination under a microscope.

Bone marrow biopsy: The removal, by a needle, of a sample of tissue from the bone. The cells are checked to see whether they are cancerous. If cancerous plasma cells are found, the pathologist estimates how much of the bone marrow is affected. Bone marrow biopsy is usually done at the same time as bone marrow aspiration.

Calcium: A mineral found mainly in the hard part of bone matrix.

Cancer: A term for diseases in which malignant cells divide without control. Cancer cells can invade nearby tissues and spread through the bloodstream and lymphatic system to other parts of the body.

Catheter: A tube that is placed in a blood vessel to provide a pathway for drugs or nutrients. The catheter allows medications, fluids, or blood products to be given and blood samples to be taken.

Cereblon E3 ligase modulators: An immunotherapy that can cause the breakdown of proteins Ikaros and Aiolos located inside myeloma cells. Through a series of subsequent events, these drugs can stimulate the immune system to kill myeloma cells.

Chemotherapy: The treatment of cancer with one or more drugs that kill all rapidly-dividing cells.

Chromosome: A strand of DNA and protein in the nucleus of a cell. Chromosomes carry genes and function in the transmission of genetic information. Normally, human cells contain 46 chromosomes.

Chronic: Persisting over a long period of time.

Clinical trial: A research study of new treatment that involves patients. Each study is designed to find better ways to prevent, detect, diagnose or treat cancer and to answer scientific questions.

- Control group – The arm of a randomized clinical trial that gets the standard treatment.
- End point – What a clinical trial is trying to measure or find out; the goal of the trial. Typical end points include measurements of toxicity, response rate and survival.
- Treatment group – The arm of a randomized trial that gets the new treatment.
- Randomized controlled trial – A research study in which subjects are randomly assigned to receive a particular treatment.

Computerized axial tomography (CAT or CT) scan: A test using computerized X-rays to create three-dimensional images of organs and structures inside the body; used to detect small areas of bone damage or soft tissue involvement.

Corticosteroids (steroids): Chemicals that are naturally produced by the adrenal gland to help prevent inflammation. Steroids are often given to cancer patients, along with one or more anticancer drugs, and appear to help to control the effects of the disease on the body.

Creatinine: A small chemical compound normally separated from blood and transferred into urine by the kidneys. If the kidneys are damaged, the serum (blood) level of creatinine builds up, resulting in an elevated serum creatinine. The serum creatinine test is used to measure kidney function.

Cytogenetics: The study of the structure of chromosomes that can help to identify genetic errors in myeloma cells. There are two main types of cytogenetics use in myeloma: karyotyping and fluorescence in situ hybridization (FISH).

Cytokine: A substance secreted by cells of the immune system that stimulates growth/activity in a particular type of cell. Cytokines are produced locally (ie, in the bone marrow) and circulate in the bloodstream.

Diagnosis: The process of identifying a disease by its signs and symptoms.

Dialysis: The process of removing waste products and excess fluid from the blood. It is necessary when a person's kidneys are unable to adequately filter their blood.

DNA: The substance of heredity; a large molecule that carries the genetic information that cells need to replicate and to produce protein.

Electrophoresis: A laboratory test in which a person's serum (blood) or urine molecules are subjected to separation according to their size and electrical charge. For people with myeloma, electrophoresis of the blood or urine allows both the calculation of the amount of myeloma protein (M-protein) as well as the identification of the specific M-spike characteristic for each individual. Electrophoresis is used as a tool for both, diagnosis and monitoring. There are two types of electrophoresis:

- Serum protein electrophoresis (SPE or SPEP)
- Urine electrophoresis (UPE or UPEP)

Enzyme: A substance that affects the rate at which chemical changes take place in the body.

Erythrocytes: Cells in the blood that contain hemoglobin and deliver oxygen to, and take carbon dioxide from, all parts of the body. Also called red blood cells (RBCs).

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

Extramedullary plasmacytoma: A collection of plasma cells found outside the central cavity (medulla) of the bone.

Free light chain: A portion of the monoclonal protein of light molecular weight that can be measured in a sensitive test: the Freelite assay.

Gene: A specific sequence of DNA or RNA; the biological unit of heredity located in a specific place on a chromosome and found in all cells in the body. When genes are missing or damaged, cancer may occur.

Genetic: Inherited; having to do with information that is passed from parents to children through DNA in the genes.

Granulocyte: A type of white blood cell that kills bacteria. Neutrophils, eosinophils, and basophils are granulocytes.

Hematocrit: Measures the proportion of blood volume occupied by red blood cells. Not a routinely used measurement in Canada but common in the USA.

Hematologic: Originating in the blood, or disseminated by the circulation or through the bloodstream.

Hemoglobin (Hb or Hgb): The substance in the red blood cell that contains iron and transports oxygen. Commonly used to monitor anemia.

High-dose therapy and stem cell transplantation: High-dose therapy is an intensive drug treatment that kills cancer cells, destroys bone marrow and can cause severe side effects. Following high-dose therapy, stem cells are used to "rescue" or rebuild the bone marrow and its blood-forming potential.

Hormones: Chemicals produced by various glands of the body that regulate the actions of certain cells or organs.

Hypercalcemia: 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 people with myeloma 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, hypercalcemia is usually treated on an emergency basis using IV fluids combined with drugs to reduce bone destruction along with direct treatment for the myeloma.

Hyperviscosity: A syndrome that results in blood that is thicker (less liquid) usually due to increased numbers of immunoglobulins.

Immunoglobulin (Ig): A protein produced by plasma cells, an essential part of the body's immune system. Immunoglobulins attach to foreign substances (antigens) and assist in destroying them. The classes of immunoglobulins are IgA, IgG, IgM, IgD and IgE.

IgG, IgA: The two most common types of myeloma. The G and the A refer to the type of protein produced by the myeloma cells. The myeloma protein, which is an immunoglobulin, consists of two heavy chains, (for example, a G type) combined with two light chains, which are either kappa (κ) or lambda (λ) Therefore, the two most common subtypes of myeloma have identical heavy chains (ie, IgG kappa and IgG lambda). The terms heavy and light refer to the size or molecular weight of the protein, with the heavy chains being larger than the light chains. Since the light chains are smaller, they are more likely to leak out into the urine, resulting in Bence-Jones protein.

IgD, IgE: Two types of myeloma that occur less frequently.

IgM: Usually associated with Waldenström macroglobulemia. In rare cases can be a type of myeloma.

Immune system: The complex group of organs and cells that produces antibodies to defend the body against foreign substances such as bacteria, viruses, toxins and cancers.

Immunofixation: A specialized type of electrophoresis that can identify the type of monoclonal paraprotein or M-protein that makes up an M-spike (ie, whether it is IgG, IgA, kappa (κ) or lambda (λ)). This immunoelectrophoresis test can be conducted on the blood (serum) or the urine.

Immunotherapy: In myeloma, immunotherapy treatments work by stimulating the body's immune system to better recognize and eliminate myeloma cells.

Induction therapy: The initial therapeutic measure in a series of treatments given in an effort to achieve remission of a disease. When used by itself, induction therapy is accepted as the best (first-line) treatment. If it doesn't cure the disease or if it causes severe side effects, other treatments may be added or used instead.

Informed consent: The process requiring a doctor to give a patient enough information about a proposed procedure for the patient to make an informed decision about whether or not to undergo it. The doctor must, in addition to explaining all procedures, address the issues of risks, benefits, alternatives and potential costs.

Interleukin: A naturally produced chemical released by the body or a substance used in biological therapy. Interleukins stimulate the growth and activities of certain kinds of white blood cells. Interleukin-2 (IL-2) is a type of biological response modifier that stimulates the growth of certain blood cells in the immune system that can fight some types of cancer. Interleukin-6 (IL-6) is a cytokine which is a potent stimulus to osteoclast and plasma cell activities.

Karyotyping: A means of looking at the chromosomes of an individual cell arranged in pairs and sorted by size. This test can detect large genetic changes, such as the existence of an extra chromosome.

Kyphoplasty: In kyphoplasty, a balloon is inserted into the compressed vertebra and inflated to raise the collapsed section. The cavity is then filled with a bone cement, stabilizing the vertebrae and preserving the reestablished height.

Lactate dehydrogenase (LD or LDH): An enzyme (protein) that helps the process of turning sugar into energy for your cells to use. It may be used to monitor myeloma activity.

Lesion: An area of abnormal tissue change. A lump or abscess that may be caused by injury or disease, such as cancer. In myeloma, "lesion" can refer to a plasmacytoma or a hole in the bone.

Leukocytes: Cells that help the body fight infections and other diseases. Also called white blood cells (WBCs).

Lymphocytes: A type of white blood cell (leukocyte) that fights infection and disease.

Lytic bone lesions: The damaged area of a bone that shows up as a dark spot on an X-ray when enough of the healthy bone in any one area is eaten away. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

Magnetic resonance imaging (MRI): A diagnostic test that uses magnetic energy, rather than X-ray energy, to produce detailed two- or three-dimensional images of organs and structures inside the body. Gives very fine resolution of soft tissues, especially encroachments on the spinal cord.

Melanoma: A cancer of the pigment-forming cells of the skin or the retina of the eye. Not associated with myeloma despite the similar-sounding name.

Minimal residual disease (MRD): Myeloma cancer cells that are resistant to treatment can be found in people in remission with no symptoms of the disease. Measuring the level of MRD may help to detect potential relapses as quickly as possible. Until recently, none of the tests used to assess or detect myeloma have been sensitive enough to detect MRD. However, now M-protein levels in the blood may be used to establish MRD.

Monoclonal: A clone or duplicate of a single cell. Myeloma develops from a single malignant plasma cell (monoclone). The type of myeloma protein produced is also monoclonal; a single form rather than many forms (polyclonal). The important practical aspect of a monoclonal protein (M-protein) is that it shows up as a sharp spike (M spike) in the serum electrophoresis test.

Monoclonal antibodies (MoAbs): Artificially manufactured antibodies specifically designed to find and bind to cancer cells for diagnostic or treatment purposes. They can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumour cells.

Monoclonal gammopathy of undetermined significance (MGUS): Condition whereby low levels of monoclonal protein are produced in the blood and/or urine.

Monoclonal protein (M-protein): Also known as monoclonal spike (M-spike), monoclonal peak (M-peak), paraprotein or myeloma protein. These are antibodies or parts of antibodies found in unusually large amounts in the blood or urine of people with myeloma. M-spike refers to the sharp pattern that occurs on protein electrophoresis when an M-protein is present (see "Monoclonal").

Myeloma defining events (MDEs): Biologic markers that indicate that smoldering mulitple myeloma (SMM) has progressed to active myeloma.

Osteoblast: The cell that produces osteoid, which becomes mineralized with calcium to form new hard bone.

Osteoclast: A cell found in the bone marrow at the junction between the bone marrow and the bone that resorbs or breaks down old bone. In myeloma, the osteoclasts are over-stimulated while osteoblast activity is blocked. The combination of accelerated bone resorption and blocked new bone formation results in lytic lesions.

Osteonecrosis of the jaw (ONJ): A previously rare jaw problem now being observed in a small percentage of people taking bisphosphonates. The condition produces pain, swelling, and bone damage around the tooth sockets in the jaws. There is bone necrosis or loss of bone which can lead to loose teeth, sharp edges of exposed bone, bone spurs and the breaking loose of small bone spicules or dead bone. A case definition is ≥3 months with non-healing exposed bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness or a “heavy jaw” feeling, or loosening of a tooth.

Osteoporosis: Reduction in bone density typically associated with old age. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

Overall survival: Length of time from either the date of diagnosis or the start of treatment when the patient is still alive.

Pheresis: A procedure that separates and filters the blood into its components.

Placebo: An inert (inactive) substance often used in clinical trials for comparison with an experimental drug.

Plasma: The liquid part of the blood in which red blood cells, white blood cells and platelets are suspended.

Plasma cells: Special white blood cells that produce antibodies. The malignant cell in myeloma. Normal plasma cells produce antibodies to fight infection. In myeloma, malignant plasma cells produce large amounts of abnormal antibodies that lack the capability to fight infection. The abnormal antibodies are the monoclonal protein, or M protein. Plasma cells also produce other chemicals that can cause organ and tissue damage (ie, anemia, kidney damage and nerve damage).

Plasmacytoma: A collection of plasma cells found in a single location rather than diffusely throughout the bone marrow, soft tissue, or bone.

Platelet cells (thrombocytes): One of the three major blood elements, others being the red blood cells and white blood cells. Platelets are the major defense against bleeding.

Positron Emission Tomography (PET scan): A diagnostic test that uses a sophisticated camera and computer to produce images of the body. PET scans show the difference between healthy and abnormally functioning tissues.

Prognosis: The projected outcome or course of a disease; the chance of recovery; the life expectancy.

Progression-free survival: The time period during which a person with myeloma survives and the cancer does not become worse. The improved survival that can be directly attributed to the treatment given for the myeloma. This term identifies people with myeloma who are in complete remission versus those who have had an episode of relapse or progression.

Protocol: A detailed plan of treatment including the dose and schedule of any drugs used.

Radiotherapy: Treatment with X-rays, gamma rays, or electrons to damage or kill malignant cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumour (implant radiation).

RANKL inhibitors: Drugs that prevent the activation of osteoclasts and reduce the process of bone breakdown by binding to a specific protein (RANKL) in the body.

Red blood cells (RBCs) or erythrocytes: Cells in the blood that contain hemoglobin and deliver oxygen to and take carbon dioxide from all parts of the body. Red cell production is stimulated by a hormone (erythropoietin) produced by the kidneys. People with myeloma who have kidney damage don't produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency.

Renal insufficiency: Reduction in kidney function.

Serum free light chain (sFLC): Light chain (kappa or lambda) portion of antibodies that are free to circulate in the blood.

Serum free light chain assays (Freelite®): A test that can be used to measure the level of free light chains in the blood.

Side effects (also know as adverse events, AEs): Problems that occur due to drugs used for disease treatment. Common side effects of cancer chemotherapy are fatigue, nausea, vomiting, decreased blood cell counts, hair loss and mouth sores.

Skeletal survey (full-body X-ray): A series of plain X-rays of the skull, spine, ribs, pelvis and long bones to look for lytic lesions and/or osteoporosis.

Smouldering multiple myeloma (SMM): Also known as indolent or asymptomatic myeloma. SMM is a generally asymptomatic precursor of myeloma where plasma cells may make up 10%-60% of the bone marrow, serum M-protein is greater than 30 g/L, and urinary M-protein is equal to or greater than 500 mg per 24 hours. However, there is still no CRAB symptoms of myeloma or MDEs.

Stem cell: An immature cell from which all blood cells develop. A normal stem cell can develop into normal blood components such as red cells, white cells and platelets. Stem cells are normally located in the bone marrow and can be harvested for transplant.

Thrombocyte: See "Platelet"

Tumour: An abnormal mass of tissue that results from excessive cell division. Tumours perform no useful body function. They may either be benign or malignant.

Vaccine: A preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms administered to produce or artificially increase immunity to a particular disease.

Vertebroplasty: A procedure that consists of injecting bone cement into the affected vertebrae to stabilize it.

Waldenström macroglobulemia: A rare type of indolent lymphoma that affects plasma cells. Excessive amounts of IgM protein are produced. Not a type of myeloma.

White blood cells (WBCs) or leukocytes: General term for a variety of cells responsible for fighting invading germs, infection and allergy-causing agents. These cells begin their development in the bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, granulocytes, lymphocytes, and monocytes.

X-ray: A quick test that uses high-energy electromagnetic radiation in low doses to produce images of the structures inside your body (ie, your bones).

Myeloma Canada

Mailing address:
Myeloma Canada
1255 TransCanada, Suite 160
Dorval, QC H9P 2V4

Telephone:
Toll-free: 1-888-798-5771

E-mail:
contact@myeloma.ca

Website:
www.myeloma.ca

Follow us on social media for the most up-to-date information and resources:

MYELOMA CANADA
MAKING MYELOMA MATTER

Charitable registration number: 862533296RR0001

© 2023 Multiple Myeloma Canada

Sixth edition: July 2023