To discuss any of the information contained in this guide, or further assistance, please call the Myeloma Support Line on 1800 MYELOMA (1800 693 566)

A Myeloma Support Nurse will answer your call in confidence
Myeloma – A Comprehensive Guide

This guide is written for people who have been diagnosed with myeloma. It will also be helpful for their families, friends and health professionals. It provides comprehensive information on myeloma and its treatment and management. The purpose of this guide is to promote a better understanding of the disease, which will enable informed decisions about care and treatment options. Being informed is a key step in learning to manage and cope. Some of the more unusual or technical words appear in **bold** the first time they are used and are described in the glossary of medical terms at the back of the guide. We recognise that not everyone requires such a comprehensive guide, particularly when first diagnosed with myeloma. A simpler myeloma guide can be found at [www.cancercouncil.com.au](http://www.cancercouncil.com.au).

**Myeloma Australia** is a national non profit organisation dedicated to providing information and support for those affected by myeloma. Founded in Victoria in 1998 by three families personally touched by myeloma, the organisation has grown to become a significant provider of services and support for the myeloma community.

Myeloma Australia:
- provides information and support to people living with myeloma, their family, friends and health professionals through its specialist myeloma support nurse led programs
- raises awareness of myeloma
- provides funding for research projects facilitated by our Medical and Scientific Advisory Group
- advocates to state and federal government for support regarding access to new therapies

To talk to someone about any aspect of myeloma, its treatment and management call the toll-free Myeloma Australia Support Line on 1800 MYELOMA (1800 693 566). The Support Line is available 9am to 5pm (AEST) Monday to Friday and a myeloma support nurse will answer the call in confidence.
Acknowledgements

This publication has been produced by Myeloma Australia with thanks to Myeloma UK whose 2006 patient guide formed the basis of this publication.

We would also like to thank reviewers of this guide: Prof Miles Prince AM (Consultant Haematologist Peter MacCallum Cancer Centre and Epworth Healthcare, Melbourne) and Dr Hang Quach (Consultant Clinical and Laboratory Haematologist, St Vincent’s Hospital Melbourne) and Helen Chapman (Editor and Consumer Representative).

ABN: 30 476 390 368
Publication date: November 2010
Updated: September 2019

Printed by Eastern Press Pty Ltd
www.epress.com.au
Contents
P4   Introduction
P5   What is myeloma?
P8   What are the different types of myeloma?
P10  What are the symptoms of myeloma?
P11  How is myeloma diagnosed?
P15  Staging myeloma
P17  What is the treatment for myeloma?
P23  What treatment will be offered first?
P26  Conventional chemotherapy based combinations
P28  Corticosteroids (steroids)
P31  Immunomodulatory drugs (IMiDs)
P31  Thalidomide (Thalomid®)
P32  Lenalidomide (Revlimid®)
P33  Pomalidomide (Pomalyst®)
P34  Proteasome inhibitor drugs
P42  Combinations of treatments
P46  High dose therapy and Autologous Stem Cell Transplantation (AuSCT)
P54  Maintenance treatment
P55  What are the treatments for symptoms and complications due to myeloma?
P55  Bone disease
P58  Pain
P58  Fatigue
P59  Kidney damage
P60  Anaemia and infections
P63  How is myeloma treated when it becomes active again?
P65  How to know if the treatment has worked?
P68  New treatments and clinical studies
P71  Living with myeloma
P74  Communication with the medical team
P76  Self help checklist
P77  Further information and useful organisations
P79  Medical terms explained
P89  Appendices
P95  Notes
P96  Contact details

Disclaimer
While the advice and information in this guide is believed to be true and accurate in the Australian setting at the
time of publication, neither the authors, neither reviewers, nor the publishers accept any legal responsibility
for the content. It is strongly recommended that advice is sort directly from medical professionals for the
correct response for individual circumstances.
Introduction

Receiving a diagnosis of myeloma can naturally be bewildering. Many may never have heard of the condition. Myeloma is a complex disease and this guide is designed to help people understand the nature of the disease, the available treatment options, signs and symptoms and how to manage with the condition.

It is important to remember that myeloma is often a slowly progressing disease and there are now many treatment options. With improvements in treatment, people are increasingly living well with myeloma for years.

We hope everyone finds this guide informative and helpful as a reference at various times throughout diagnosis and treatment. There is a page to record useful contact numbers and a notes page to write questions for the medical team.

It is beyond the scope of any guide to include everything there is to know and understand about myeloma. We have therefore made note within the guide to further reading and information resources available by Myeloma Australia and other organisations, for those interested in learning more.

Myeloma Australia has resources, information and support to assist those living with myeloma at any time. The Myeloma Support Nurses are there to speak to patients, family members, carers, friends and health professionals. Call 1800 MYELOMA (1800 693 566) Monday to Friday 9am – 5pm AEST or visit the website for many more resources.
What is Myeloma?

Myeloma, also known as multiple myeloma, is a type of bone marrow cancer arising from plasma cells, which are normally found in the bone marrow. Plasma cells form part of our immune system.

Normal plasma cells produce antibodies (also called immunoglobulins) to help fight infection. In myeloma, the abnormal plasma cells release only one type of antibody known as the monoclonal (M) protein or paraprotein, which has no useful function. It is often through the measurement of this paraprotein that myeloma is diagnosed and monitored.

Bone marrow is the ‘spongy’ material found in the centre of larger bones in the body (see Figure 1). As well as being home to plasma cells, the bone marrow is the centre of blood cell production (red blood cells, white blood cells and platelets).
In myeloma, the DNA of a plasma cell is damaged causing it to become malignant or cancerous. These abnormal plasma cells are known as myeloma cells. Unlike many cancers, myeloma does not usually exist as a lump or tumour. Instead, the myeloma cells usually divide and expand within the bone marrow.

Myeloma affects multiple places in the body (hence multiple myeloma) where bone marrow is normally active in an adult, i.e. within the bones of the spine, skull, pelvis, the rib cage, shoulders and hips.

The areas usually not affected are the extremities: that is the hands, feet, and lower arm / leg regions. This is very important since the function of these critical areas is usually fully retained.

Most of the medical problems related to myeloma are caused by the build up of myeloma cells in the bone marrow and the presence of the paraprotein in the blood or in the urine.

Common problems are bone pain, bone fractures, tiredness (due to \textit{anaemia}), frequent or recurrent infections (such as bacterial pneumonia, urinary tract infections and shingles), kidney damage, and elevated \textit{calcium} in the blood (\textit{hypercalcaemia}).

A small percentage of people go on to develop myeloma after having been diagnosed with a benign (non malignant) condition called \textit{MGUS} which stands for Monoclonal Gammopathy of Undetermined Significance. This term describes the condition of the raised abnormal protein seen in myeloma (the paraprotein), but where there are no other features of the disease (less than 10% plasma cells in bone marrow and no evidence of bone disease).

The risk of transition from MGUS to active myeloma is very low: only a 1% chance each year of follow up.

Even if the myeloma cells are at a higher level of 10-30% of the total bone marrow, their rate of growth can be very slow and represents \textit{asymptomatic} (also known as indolent or \textit{smouldering}) myeloma.

Both these conditions can change very slowly over a period of years and do not require active treatment. It is very important to establish the correct diagnosis distinguishing MGUS and asymptomatic myeloma from active or symptomatic myeloma, which does require treatment.
Treatments for myeloma can be very effective at halting its progress, controlling the symptoms, and improving quality of life, but they are not able to cure it. Even after successful treatment, regular monitoring is needed for when the myeloma returns (relapse). If the myeloma is under control people usually return to a good state of health which can last from months to years.

The outlook for myeloma is improving with many new developments in the treatment and management having had a significant impact on improved outcomes. Research is ongoing to develop new treatments and to use existing treatments in a better, more effective way. Many of the current and new developments are discussed in this guide.

**Basic Facts:**

- There are approximately 1,800 new cases of myeloma per year in Australia
- Over 15,000 people are living with myeloma at any one time
- Slightly more males than females will have myeloma
- Myeloma accounts for 15% of blood cancers and 1% of cancers generally
- Median age of onset is 70 and only 5-10% of patients are under 50

Further information about living with myeloma can be obtained by accessing one or more of the many services offered by Myeloma Australia. In the first instance, contact one of the Myeloma Support Nurses on 1800 MYELOMA (693 566) or visit www.myeloma.org.au

**MGUS**
- Paraprotein <30g/L or abnormal free light chain ratio
- <10% plasma cells in the bone marrow
- No symptoms of myeloma

**Asymptomatic Myeloma**
- Paraprotein >30g/L
- 10 – 60% plasma cells in the bone marrow
- No symptoms of myeloma

**Symptomatic Myeloma**
- Measurable paraprotein
- >10% plasma cells in the bone marrow
- Symptoms of myeloma
What are the different types of myeloma?

Myeloma is often described as being a very individual disease; both in terms of the way those affected experience complications and in the way they respond to treatment, all of which can vary greatly. Some of this variation is due to the different types and subtypes of myeloma.

Different types and subtypes of myeloma are based on the type of immunoglobulin (paraprotein) produced by the myeloma cell.

Each immunoglobulin is made up of a specific structure containing two principal components, heavy chains of which there are two, and light chains of which there are also two (see Figure 2).

There are five possible types of heavy chain component denoted by the letters G, A, D, E and M, and there are two possible types of light chain component denoted by the Greek letters, Kappa (ƙ) and Lambda (ƛ).

Each individual immunoglobulin (Ig for short), can have only one of the five possible heavy chain types and only one of the two possible light chain types.

Most people with myeloma, about 65%, have what is called IgG type myeloma. That is immunoglobulin type G (one of the five possible heavy chains), with either the kappa or lambda light chain component.

The next most common type is IgA myeloma also with either kappa or lambda light chains. IgM, IgD and IgE type myeloma are all quite rare.

At the same time as producing one whole immunoglobulin structure, approximately 30% of patients will also produce light chains (such as kappa light chains) on their own, which are detectable in the urine rather than in the blood.
In about 20% of patients, the myeloma cells produce light chains only (no heavy chains at all). This is called light chain or Bence Jones myeloma.

More rarely, in about 1-2% of cases, the myeloma cells produce very little or no immunoglobulin of any type. This is known as non secretory myeloma making diagnosis and monitoring very difficult. However, a test called the Freelite™ test is able to detect minute amounts of light chains in the blood in most of the patients traditionally labelled as having non secretory myeloma, therefore making diagnosis and monitoring easier. If no light chains are detected using the Freelite™ test then people with non secretory myeloma will have their disease monitored via bone marrow aspirate and trephine (BMAT) biopsies or if bone disease is a feature, scans can help monitor the disease.

In some cases abnormal plasma cells may collect in the bone or tissue forming what’s known as a plasmacytoma. This can occur in addition to other features of myeloma or on its own which is referred to as a solitary plasmacytoma. Radiotherapy can be used to treat a plasmacytoma.

The light chain or Bence Jones myelomas are the types most likely to cause kidney damage. If light chains deposit in the kidneys, nerves or other organs it can result in a conditions known as AL amyloidosis or light chain deposition disease.

Regular measurements of the paraprotein are taken to help confirm a diagnosis and determine the subtype of myeloma. Measurements are also taken during the course of the disease to help determine the response to any given therapy and for periodic restaging of the disease.

**What Causes Myeloma?**

Although there has been a large amount of research to investigate the potential triggers of myeloma, nothing has been proven to date.

Exposure to certain chemicals, radiation, viruses and a weakened immune system are thought to be potential causal or trigger factors. It is likely that myeloma develops when a susceptible individual has been exposed to one or more of these factors.

Because it is more common to develop myeloma later in life, it is thought that susceptibility may increase with the ageing process and the associated
reduction in immune function, or that myeloma may result from a lifelong accumulation of exposure to toxic substances or immune system challenges. There is a rare tendency for myeloma to occur in families, but the likelihood is very low, and no tests are currently available for screening of this. Even when myeloma occurs more than once within a family, this may be due to a common exposure to environmental factors, rather than it being hereditary.

**What are the symptoms of myeloma?**

Myeloma can cause a range of symptoms because of its effect on the bones, bone marrow and kidneys. In some people there are no symptoms at diagnosis or in the early stages. When present, symptoms may be vague and similar to those of other conditions. Some of the more common symptoms are:

- Bone pain or a broken bone that has not been caused by obvious injury
- Fatigue and general weakness
- Frequent or prolonged infections
- Loss of appetite and weight loss
- Kidney impairment
- Increased thirst, confusion and nausea – caused by a high level of calcium in the blood

More about managing these symptoms is covered later in this guide.
How is myeloma diagnosed?

Common tests and investigations

In order to diagnose myeloma, several tests and investigations are needed. This is often a difficult and uncertain time for those affected by myeloma and their families. Tests and investigations are carried out for three main reasons:

- To establish a diagnosis and extent of the disease
- To help determine a treatment plan and monitor progress
- To detect complications of the disease

Myeloma is a very individual disease and test results may vary from person to person. It is not enough just to make a diagnosis of myeloma; it is critical to have an accurate picture of the disease in each person affected before an appropriate treatment plan can be developed.

Paraprotein measurement

As well as being important in diagnosing myeloma, changes in the level of paraprotein (in the blood and/or urine) are usually a fairly good indicator of changes in the activity of the myeloma. For this reason, paraprotein measurements are done regularly at intervals determined by the doctor (e.g. monthly or 3 monthly) to see how well the treatment is working and to check that the myeloma is remaining stable during periods between treatments.

If no paraprotein is detectable after treatment it is considered a complete response (CR) has occurred. If the paraprotein has fallen and is still detectable and stable after treatment it is considered a partial response (PR).

A stable, low level of paraprotein maintained over a period of time is often described as plateau phase. The term ‘plateau phase’ is used because a graph of the paraprotein results appears flat like a plateau. Both the level and duration of response are important when measuring how successful treatment has been. Further information on measuring response to treatment can be found in the ‘Treatment’ section of this guide (see Table 8 Response Criteria).

In about 20% of people with myeloma, the abnormal paraprotein is detected in the urine where it is known as Bence Jones protein. A test called a 24hr urine collection may be used to measure the Bence Jones protein.
Paraprotein can be measured by a simple blood or urine test in the following ways, depending on the type of myeloma:

**Blood tests:**
- Serum protein electrophoresis (SPEP)
- Immunofixation electrophoresis (IFE)
- Immunoelectrophoresis (IEP)
- Serum Free Light Chain (SFLC)

**Urine test:**
- 24 hr urine collection for Bence Jones Protein

**Imaging of the bones**

Because myeloma can thin or erode the bones, it is important that the bones of the body are assessed, there are a number of imaging techniques (scans) that can be used to do this. The medical team may request a single type of scan or more than one. The most commonly used imaging scans for assessing myeloma are:

- A whole body low dose CT (Computerised Tomography) skeletal survey is preferred over X-ray skeletal surveys as they are more accurate at identifying myeloma related bone changes and bone damage known as ‘lytic lesions’.
- MRI (magnetic resonance imaging) scans can also be used as they can show the presence and distribution of myeloma in the bone, bone marrow and sometimes outside the bone, as well as allowing assessment of the spinal cord in special situations.
- A sestamibi and a PET (Positron Emission Tomography) scan use an injection of a radiolabeled marker to help detect areas of active myeloma that may not be detected by other imaging techniques.

It is important to note that PET scans are not routinely reimbursed by medicare for myeloma and there may be out of pocket costs which may vary between different treatment centres.

**Bone Marrow Aspirate and Trephine Biopsy (BMAT)**

This involves putting a needle into bone (usually the pelvic bone) to get a small sample of the bone marrow (sometimes called an aspirate), and is done under a local anaesthetic. This sample is then examined to count the
percentage of plasma cells present in the bone marrow: normal bone marrow has fewer than 5% plasma cells; bone marrow in people with myeloma may have between 10% and 90% plasma cells. This test may also be done at the beginning and end of each course of treatment.

A better indication of the number of plasma cells is gained by doing a ‘trephine biopsy’ which means taking a small core of bone along with the marrow inside. Together with blood and/or urine sampling these tests help to give a more comprehensive picture of response to treatment.

**Cytogenetic testing**

Analysis of the **chromosomes** (the structures that carry genetic information in cells) found in the bone marrow samples can reveal good or poor chromosomal features. During mutation, chromosomes can be gained (additional), be left out (deletion) or break off and reattach elsewhere (translocation). Cytogenetic results may be useful to guide treatment choices in those with high risk disease. Chromosomal abnormalities that seem to be related to a higher risk myeloma are termed t(4;14), t(14;16), t(14:20);del 17p and 1q21 amplification.

Researchers are currently exploring the relationship between different cytogenetic abnormalities and treatment outcomes.

**Molecular testing**

Analysis for molecular gene mutations or changes in the number of individual gene numbers can now be tested. It is used routinely in the management of leukaemias and is an area of active investigation in myeloma. The doctor may discuss with you the testing of these mutations on a bone marrow specimen. Currently it is not considered standard-of-care.

**Full blood count**

Throughout treatment, regular blood samples are taken. As has already been mentioned, blood samples are used to measure the level of paraprotein present in the blood.

In addition, part of every sample is normally used to count the make up of some of the important cells in blood; the red blood cells, which transport oxygen; white blood cells, which help fight infection; and platelets, which help the blood to clot.
These cell counts are important because:

- The white cell count indicates the risk of infection
- The haemoglobin level (red cell count) detects anaemia
- The number of platelets indicates the risk of bleeding or bruising more easily than normal

**Kidney function**

Kidney function can be affected by certain unique features associated with myeloma and also from the side effects of some treatments.

Blood tests are also used to help measure levels of urea and creatinine, which are waste products that are normally filtered out by the kidney. High levels of urea and creatinine indicate poor kidney function.

**Calcium measurement**

Calcium is a mineral normally found in the bone. In patients with active bone disease due to myeloma, calcium is released from the bone into the bloodstream, which can lead to higher levels of calcium in the blood (hypercalcaemia).

**Albumin measurement**

Albumin is a type of protein that normally makes up most of the protein found in the blood, but in myeloma, hormones (or cytokines) produced by the myeloma (mainly interleukin 6; IL 6) can suppress albumin production.

**Beta 2 microglobulin (β2M)**

β2M is a molecule that sits on the cell surface of lymphocytes. Plasma cells are a type of lymphocyte and myeloma cells express β2M on their surface. β2M is one of the most important indicators of both the amount and activity of the myeloma and therefore is crucial measurement in staging of the disease.

**Lactate Dehydrogenase (LDH)**

LDH is an enzyme found in nearly all living cells. If cells are destroyed, LDH is released into the blood stream. The LDH level can help determine the aggressiveness of myeloma as rapid plasma cell growth death can cause an elevation of LDH.
Lab Tests Online is a useful website resource to search for up to date information on laboratory tests and how they are used. 
www.labtestsonline.org.au

The appendix at the back of this guide includes a list of potential tests as well as some of the normal values

**Staging myeloma**

Completion of a wide range of tests gives a clear and in depth picture of the specific characteristics of an individual’s myeloma. With this information, the myeloma can be staged.

Staging indicates the amount of myeloma and therefore reflects the expected outlook for individual patients. The current International Staging System (ISS) for myeloma takes into account important factors such as $\beta_2$M and albumin. Both these factors can be assessed by a simple blood test.

**Revised International Staging System (R-ISS)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| R-ISS I | Serum albumin $\geq$35g/L  
AND  
$\beta_2$M of $< 3.5$mg/L  
Normal LDH  
AND  
No abnormal cytogenetics |
| R-ISS II| Neither I or III                                                           |
| R-ISS III| Serum $\beta_2$M of $\geq 5.5$mg/L  
AND  
High LDH  OR High risk cytogenetics |
To help identify a person with myeloma that requires treatment, doctors often use criteria summarised by the acronym ‘**CRAB**’:

<table>
<thead>
<tr>
<th>C</th>
<th>Calcium elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Renal (kidney) insufficiency/failure</td>
</tr>
<tr>
<td>A</td>
<td>Anaemia</td>
</tr>
<tr>
<td>B</td>
<td>Bone abnormalities/disease (lytic lesions or bone loss)</td>
</tr>
</tbody>
</table>

The CRAB criteria helps doctors determine if the myeloma is having an adverse effect on the body and therefore decide the optimal time to start treatment. The term **Myeloma Defining Events** is also used and refers to a very similar set of clinical features.

Note that while staging myeloma tells doctors how advanced the myeloma is, it does not predict the outcome of treatment. Even with advanced myeloma, successful treatment approaches are available.
What is the treatment for myeloma?

Although myeloma remains an incurable disease, outcomes have improved significantly, owing to the introduction of improved treatment options. Firstly, the use of high dose therapy and autologous stem cell transplant (AuSCT) in the late 1990’s, then novel therapeutic agents in particular thalidomide (Thalomid®), bortezomib (Velcade®) and lenalidomide (Revlimid®). This increase in range of treatment options means there are an increasing variety of different treatment combinations. The choice of best treatment will be tailored to each individual and what may suit one person with myeloma may not be the best option for another.

The likely course of the disease in those with myeloma is one of active treatment followed by periods of remission or stable disease where no treatment is required. During this time the haematologist / oncologist will be actively monitoring the blood and general health for signs of the myeloma returning or becoming more active. It is likely that a range of different treatment types will be used over time.

The next few sections look at some important points in making treatment decisions and provide a brief overview of the range of treatments available to treat both the underlying problem and the complications and symptoms due to myeloma.

Decision making

Choosing treatment for myeloma is not a simple decision as no one treatment has been identified as being the best, and all people are different.

The advantages, disadvantages and side effects arising from available treatments are often quite different. For this reason, being involved in deciding which treatment is best suited is very important.

Generally, treatment options will take account of:

- General health (for example, kidney function)
- Age
- Personal circumstances and lifestyle
- Priorities and preferences
- The nature of the disease
- Level of complications or side effects
• Any previous treatments or illnesses
• Results and response to any previous treatment received

**Making an informed decision**

Making an informed decision is important and as much time should be taken as needed. However, in some situations there may be an urgent need to start treatment, for example if there is significant kidney damage.

To get a better understanding of myeloma and the treatment options available it is a good idea to read credible resources. Information is available from doctors, nurses, Myeloma Australia, other support organisations such as the Cancer Council and the Leukaemia Foundation, and the Internet (a list of reliable websites is provided on p77).

Listing the pros and cons of each option is a good way to help decide the best treatment. Talking things over with family, friends or other people with myeloma can help clarify and gain perspective. Myeloma Australia holds Information and Support Groups around Australia. These meetings are a fantastic way to connect with the myeloma community.

Decisions should take into account personal priorities and lifestyle. Each treatment choice will have benefits and difficulties including potential side effects. It is important to ensure that there is an open discussion with the treating doctor and that each party agrees with the plan.

**Second opinions**

The way cancer services are currently organised in Australia means that each hospital should involve a range of healthcare professionals working together as a team, known as a multidisciplinary team. Treatment is likely to have been discussed by the team, although often only one doctor (usually the consultant haematologist) will manage each case.

Because myeloma is not common, and choosing the right treatment is sometimes complex, a second opinion may be required to ensure that the diagnosis is correct, that the treatment plan is appropriate and that all other options have been considered.

Doctors are generally happy for a second opinion to be sought and a request for such will not cause offence to him/her or the medical team. The doctor or GP may be able to recommend another myeloma specialist and provide
a written referral letter outlining the individual’s current situation and plan for management.

**Choosing a non-conventional (alternative) approach to therapy**

Some people feel that they do not want to have any type of treatment because of fear of side effects and prefer to try an alternative approach such as dietary control. Unfortunately, there is no evidence that these alternative approaches work.

It is important to remember that conventional treatments have been well tested in clinical studies and doctors have a clear understanding of how they work. The same cannot be said for alternative approaches. If an alternative method is preferred to control the disease, it is important to discuss the potential risks with a doctor. The medical team will need to be aware of any alternative methods used, particularly should conventional treatment be chosen at a later date. Some people may want to include a complementary therapy to their conventional treatment. In some cases this is perfectly safe but there is also a risk that a complementary therapy may interact with or prevent the conventional treatment from working properly. It is important that the doctor knows exactly what is being taken to allow for the best possible outcomes.

See our Living Well with Myeloma book and Complementary Therapy fact sheet for more information

www.myeloma.org.au – 1800 MYELOMA (693 566)

**Choosing not to accept active treatment**

If a person decides not to accept any active treatment for myeloma there are many supportive measures available to help alleviate the symptoms of the disease.

If specialist advice is needed with regard to symptoms such as pain, it may be helpful to utilise a **palliative care** specialist, who will be able to provide expertise in symptom control.

**Indications for starting treatment**

Before embarking on treatment, important decisions need to be made about what treatment is best or most appropriate and when to receive it.
The decision to start or not to start treatment is an important one. Not everyone diagnosed with myeloma will need treatment to control his or her myeloma immediately.

Because currently available treatment is not curative and has side effects it is usual to wait until the myeloma is actively causing problems before starting treatment. Results from the tests and investigations listed earlier, along with other individual factors, will help determine when treatment should begin, what that treatment should be and provide a baseline against which response to treatment and disease progression can be measured.

**What treatments are available?**

There is no one standard treatment for myeloma, therapy is tailored to each person. With that in mind, the treatment and management of myeloma can be thought of as being organised into four categories. These are:

- Active monitoring
- Treatments to control the myeloma itself
- Treatments for the symptoms and complications caused by the myeloma (supportive measures)
- Treatment when the disease comes back (relapse)

There is some overlap between these categories, since any treatment that controls myeloma will have the added benefit of reducing the complications and symptoms experienced.

Treatments to manage myeloma are broadly summarised in the following table before being discussed in more detail separately.
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional standard dose chemotherapy</strong></td>
<td>The use of chemotherapy drugs, alone or in combination, to kill cancer cells. Most commonly used are melphalan and cyclophosphamide. These drugs are often used in combination with other anti myeloma treatments</td>
</tr>
<tr>
<td><strong>Immunomodulator (IMiD) based combinations</strong></td>
<td>Immunomodulator drugs (IMiDs) are given in tablet form. Shown to be effective against myeloma alone, or more commonly in combination with corticosteroids with or without chemotherapy. These drugs include thalidomide (Thalomid®), lenalidomide (Revlimid®) and pomalidomide (Pomalyst®)</td>
</tr>
<tr>
<td><strong>Proteasome inhibitor based combinations</strong></td>
<td>Proteasome inhibitor drugs such as bortezomib (Velcade®), carfilzomib (Kyprolis®) and ixazomib (Ninlaro®) are shown to be effective against myeloma, alone or more commonly in combination with corticosteroid +/- chemotherapy.</td>
</tr>
<tr>
<td><strong>Corticosteroids (steroids)</strong></td>
<td>Dexamethasone or prednisolone. Active against myeloma. Can be used alone but more commonly in combination with chemotherapy and another antimyeloma agent (thalidomide, bortezomib, lenalidomide)</td>
</tr>
<tr>
<td><strong>High dose chemotherapy and stem cell transplant</strong></td>
<td>The use of high doses of chemotherapy followed by blood stem cells to replace healthy cells damaged by the chemotherapy</td>
</tr>
</tbody>
</table>
Radiation therapy
The use of high energy X-rays to damage myeloma cells

Supportive therapy
Therapies to alleviate symptoms and manage complications of the disease and its treatments. For example:

- **Bisphosphonates** – to manage bone disease
- **Antibiotics** – to treat or prevent infections
- **Growth factors** – to boost blood cell counts
- **Immunoglobulin Infusion** – to boost levels of healthy immunoglobulins and help prevent infections
- **Blood and platelet transfusions** – to support lowered blood counts
- **Anticoagulants** – reduce risk of blood clots associated with certain anti myeloma medications
- **Pain killers** – to manage pain
- **Dialysis** – to filter a person’s blood when the kidneys are unable to do so effectively

The following sections describe the various treatments that are available in more depth and some of the circumstances under which particular treatments are used.

The Medical & Scientific Advisory Group (MSAG) of Myeloma Australia publish Clinical Practice Guidelines for the management of Multiple Myeloma. This document was written to help guide specialists and other health professionals in the management of myeloma. They are written specifically for medical professionals, are regularly updated and are available on the Myeloma Australia website: [www.myeloma.org.au](http://www.myeloma.org.au).
What treatment will be offered first?

Initial treatment

Once it is decided that treatment is required to control the disease, both doctor and patient will determine the most suitable regime. It is important to remember that, although these treatments can be very effective to control the myeloma, even over long periods of time, they do not cure the disease.

The main treatment decision at diagnosis is to decide upon pathway 1 or 2, which are broadly termed as intensive or less intensive pathways.

1. Intensive Pathway

Initial treatment plus high dose chemotherapy and autologous stem cell transplantation (AuSCT). This is the standard upfront pathway for younger, fit people, biological fitness is a more important determinant than age.

2. Less intensive Pathway

Initial treatment without high dose chemotherapy and stem cell transplantation. This is the standard upfront pathway for those older or less fit people.
Figure 3. For common combinations of therapy please see Table 4
Most often, the initial treatment includes a triplet combination of a chemotherapy drug, a steroid and a targeted drug such as lenalidomide or bortezomib (common combinations listed in Table 4). Combinations of drugs are used as each type of drug works differently to kill myeloma cells with the combined effect providing a higher chance of eradicating as much disease as possible.

Treatments are prescribed using protocols. These outline the combination of drugs used, dose according to height/weight or body surface area and the timing of doses. A course of treatment usually lasts for several months. It is given in cycles, i.e. a dose or a few days of treatment, followed by several days or weeks without treatment before the next dose is given. The exact details of the treatment schedule vary depending on the individual and type of chemotherapy and medications required, the specialist is the best person to answer specific questions about treatment schedules.

Common treatment protocols are available from the Cancer Treatments Online page of the Cancer Institute of NSW website: www.eviQ.org.au

The total length of the treatment course often depends on which medication(s) are prescribed and the response to treatment, but is likely to last between 3 and 12 months.

In the sections below, the different medications used initially to treat myeloma are described and some common combinations listed. Some possible reasons why an individual would have one treatment combination over another are also described.
Conventional Chemotherapy Based Combinations

What is chemotherapy?
Chemotherapy drugs include a range of potent drugs that are intended to kill the myeloma cells in the bone marrow. Chemotherapy works by damaging myeloma cells and preventing them from being able to divide and reproduce. Chemotherapy drugs attack cells in the body that divide rapidly, such as myeloma cells, but also may affect other rapidly dividing cells such as those in the bone marrow, hair follicles and the lining of the mouth and the stomach. Unfortunately this means that chemotherapy treatment can have side effects.

How is chemotherapy given?
Some chemotherapy drugs can be taken by mouth (oral) and others are given as an infusion into a vein (intravenous infusion or IV) or under the skin (subcutaneous or SC). Oral chemotherapy treatments can be taken at home, but hospital visits are required to receive the intravenous chemotherapy.

The type of chemotherapy prescribed for myeloma depends on the individual and what is most suitable for them and their disease at any particular point in time. Common types used to manage myeloma include melphalan and cyclophosphamide, although others are also used in certain cases.

Although chemotherapy can be given on its own as a treatment, it is more commonly given in combination with steroids, most commonly dexamethasone or prednisolone. The newer drugs thalidomide, bortezomib or lenalidomide, may also be given in combination with steroids, with or without chemotherapy. See Table 4 for some common combinations.

What are the possible side effects of chemotherapy?
Each different type of chemotherapy drug has its own side effects, and even the same kind of chemotherapy produces different reactions in different people. It may be helpful to remember that almost all side effects are only short term, are usually easily managed and should gradually disappear once the treatment has stopped.
Some of the most common side effects of many chemotherapy drugs are nausea and/or vomiting, hair loss (alopecia), sore mouth (or mouth ulcers) and diarrhoea. Certain kinds of chemotherapy can cause infertility. If preserving fertility is a priority for any individual, a discussion must take place with the doctor before treatment starts.

Information leaflets outlining the side effects of each drug are readily available from the doctor, nurse or pharmacist providing treatment.

Report side effects to the medical team straight away so they can be addressed effectively. Supportive medications to minimise side effects can be given and in some circumstances, doses and scheduling of treatment can also be altered to manage side effects.

A comprehensive guide on chemotherapy is produced by the Cancer Council and can be found on their website or by calling 13 11 20.

Treatment Fact Sheets on each of the myeloma specific drugs and can be found on the Myeloma Australia website www.myeloma.org.au

The Cancer Institute NSW – ‘eviQ – Cancer Treatments Online’ produces a range of information fact sheets on different chemotherapy drugs, common protocols and common side effects of chemotherapy that can be accessed on their website. www.eviq.org.au
Corticosteroids (steroids)

What are steroids and how do they work?
Steroids are hormonal substances naturally produced in the body. There are many different types of synthetically made steroids used to manage a range of disorders. Those used in the treatment of myeloma are known as glucocorticoids. These steroids can modify the body’s immune responses, suppress inflammation and cause myeloma cells to die.

How are steroids given?
The two most commonly used steroids in myeloma are dexamethasone and prednisolone. Steroids can be given on their own as a treatment for myeloma but are more commonly used in combination with chemotherapy or other anti myeloma drugs. Although they can be given as an infusion into a vein, they are more commonly given as a course of tablets. Tablets should be taken with food or milk to help protect the stomach from irritation. As the doses used in myeloma are often high, several tablets may be needed to be taken at one time.
Steroid treatment in myeloma is typically given in high doses but for short periods only.

What are the possible side effects of steroids?
Side effects do vary according to the dose and duration of treatment. It is important to remember that each person’s reaction to steroids may be different and that side effects, if any, are temporary and should resolve when the steroids are stopped.

Learning from experience
Side effects related to steroids often follow a very predictable pattern. Learning the pattern of side effects over a treatment cycle or period of time can be helped by keeping a side effect journal. Once the pattern of side effects has been found it is possible to work towards finding ways to manage these.
More common side effects of steroids are:

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastritis</strong></td>
<td>• Take with or after food or milk</td>
</tr>
<tr>
<td><strong>Stomach irritation or pain</strong></td>
<td>• Medication to prevent stomach irritation may be prescribed</td>
</tr>
<tr>
<td></td>
<td>• Inform the doctor if heartburn or stomach pain is experienced</td>
</tr>
<tr>
<td><strong>Mood and energy changes often related to the days steroids are taken</strong></td>
<td>• Commonly heightened mood and energy on steroid days and lower mood and energy on days immediately following steroid dose</td>
</tr>
<tr>
<td><strong>Mood swings</strong></td>
<td>• Inform family and friends of such side effects to help them understand the altered behaviour</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>• Some people find taking exercise, even a good walk, can help minimise agitation and irritability</td>
</tr>
<tr>
<td><strong>Tearfulness</strong></td>
<td>• Talk with the doctor if mood changes are acute or unmanageable</td>
</tr>
<tr>
<td><strong>Difficulty sleeping</strong></td>
<td>• Take in the morning to avoid sleeplessness</td>
</tr>
<tr>
<td></td>
<td>• Some people find sleeping tablets are helpful on the days they take steroids</td>
</tr>
<tr>
<td><strong>Increased or unstable blood glucose levels</strong></td>
<td>• Monitor blood glucose level closely, especially if diabetic</td>
</tr>
</tbody>
</table>
| Let down effect                                                                 | • Feeling of low mood and energy in the days following steroid dose  
|                                                                              | • May require tapering of steroid doses if severe  
|                                                                              | • Some people have found that drinking isotonic (sports) drinks can help reduce the ‘hangover effect’ on the days following steroid dose  
|                                                                              | • Manage lifestyle and activities around energy levels  
| Neutropenia; Increased risk of infection due to lowered white cells and neutrophils | • Be aware of common signs of infections such as temperature above 38°C, having a productive cough, having shivers or chills, swelling or inflammation at site of cut or injury  
|                                                                              | • Report any signs of infection to a GP or a specialist  
| Increased appetite                                                           | • Adopt healthy snacking to avoid weight gain  
|                                                                              | • See a dietician for further advice  
| Flushing of face                                                              | • Commonly on day of taking steroid  

See our Steroid Treatment Fact Sheet for more information.  
www.myeloma.org.au – 1800 MYELOMA (693 566)
Immunomodulatory Drugs (IMiDs)

How do IMiDs work in myeloma?
Drugs in this family include thalidomide (Thalomid®), lenalidomide (Revlimid®) and pomalidomide (Pomalyst®).
IMiDs work in a different way to conventional chemotherapy drugs. Their exact mechanism of action is the subject of ongoing research. It is likely that they:
1. Suppress the growth and survival of myeloma cells and also directly kills myeloma cells
2. Inhibit the growth of new blood vessels (angiogenesis), which myeloma cells need to grow and survive
3. Stimulate the body’s immune system to attack myeloma cells
4. Block the activity of chemicals involved in the growth and survival of myeloma cells
It seems likely that some or all of these ways of working are relevant to how the drugs in the IMiD group can be effective against myeloma.

The Australian Pharmaceutical Benefits Scheme reimburse each IMiD according to the clinical situation. The doctor will advise which drug is most appropriate within these guidelines at each time point.

Thalidomide (Thalomid®)
Thalidomide is a drug used in a variety of combinations and at various times during the course of the disease. It can either be used as part of the first line of therapy (upfront therapy) or after the myeloma has become active again after a period of control (relapse).

How is thalidomide taken?
Thalidomide is given as a daily capsule which is normally taken in the evening as it can cause drowsiness. It can be used on its own, or more commonly in combination with a steroid (dexamethasone or prednisolone) and a chemotherapy drug (melphalan or cyclophosphamide). Some of the combinations commonly used are listed in Table 4.
What are the potential side effects of thalidomide?

Side effects vary according to the dose and duration of treatment. It is important to remember that each person’s reaction to thalidomide may be different and that side effects, if any, are temporary and should resolve or diminish when the thalidomide is stopped.

Thalidomide can cause a range of side effects; the more common ones are:

- Sleepiness
- Constipation
- Rash
- Peripheral neuropathy
- Thrombosis (blood clots)
- Low blood pressure; feeling dizzy or faint, especially when standing too quickly

See Table 3 for more details of each side effect. It is important to inform the doctor or nurse if any side effects are experienced.

See our Thalidomide Treatment Fact Sheet for more information.

www.myeloma.org.au – 1800 MYELOMA (693 566)

Lenalidomide (Revlimid®)

Lenalidomide is chemically similar to thalidomide but works through a different mechanism. It often works even if thalidomide has been used previously.

How is lenalidomide taken?

Lenalidomide is given as a tablet 21 days out of every 28, in the pattern 3 weeks of treatment and 1 week rest. The starting dose is usually 25mg per day but may be reduced in the presence of complications such as kidney impairment or low blood counts. The treatment is ongoing until either the myeloma stops responding or any side effects make lenalidomide an unsuitable option.

Lenalidomide can be given as treatment on its own but more commonly is given in combination with a steroid such as dexamethasone or prednisolone. See Table 4.
What are the potential side effects of lenalidomide?

Lenalidomide is generally well tolerated and has fewer side effects than thalidomide. The most common side effects are:

- Lowered red cell count (anaemia)
- Lowered platelet count (thrombocytopenia)
- Lowered white cell count (neutropenia)
- Gastrointestinal problems; nausea, vomiting, diarrhoea and constipation
- Fatigue
- Thrombosis

See Table 3 for more details of each side effect. It is important to inform the doctor if any side effects are experienced.

See our Lenalidomide Treatment Fact Sheet for more information.

www.myeloma.org.au – 1800 MYELOMA (693 566)

Pomalidomide (Pomalyst®)

Pomalidomide is a third generation IMiD that works in similar ways to thalidomide and lenalidomide. It can work even if there has not been a previously favourable response to thalidomide or lenalidomide.

How is pomalidomide taken?

Pomalidomide is given as a tablet 21 days out of every 28, in the pattern 3 weeks of treatment and 1 week rest. The starting dose is usually 4mg per day but may be reduced in the presence of complications such as kidney impairment or low blood counts. The treatment is ongoing until either the myeloma stops responding or any side effects make pomalidomide an unsuitable option.

Pomalidomide is given in combination with a steroid such as dexamethasone or prednisolone. See Table 4.

What are the potential side effects of pomalidomide?

Pomalidomide is generally well tolerated and has similar side effects to lenalidomide. The most common side effects are:
• Lowered red cell count (anaemia)
• Lowered platelet count (thrombocytopenia)
• Lowered white cell count (neutropenia)
• Gastrointestinal problems; nausea, vomiting, diarrhoea and constipation
• Fatigue
• Thrombosis

See table 3 for more details of each side effect. It is important to inform the
doctor if any side effects are experienced.

See our Pomalidomide Treatment Fact Sheet for more information.

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Proteasome Inhibitor Drugs (PIs)

Proteasome inhibitors work in a different way to chemotherapy and the IMiD
drugs. Proteasomes are present in all cells and help regulate cell function and
growth. Proteasome inhibitor drugs include bortezomib (Velcade®), carfilzomib
(Kyprolis®) and ixazomib (Ninlaro®). These drugs interfere with the way protea-
somes work, causing cancer cells to stop growing and die. Cancer cells appear
to be more sensitive to the effects of these drugs than healthy cells.

The Australian Pharmaceutical Benefits Scheme reimburses bortezomib and
carfilzomib at certain time points. The doctor will advise when bortezomib is the
best treatment option. At the time of writing ixazomib is not yet reimbursed but
may be available through clinical trials or compassionate access schemes.

Bortezomib (Velcade®)

Bortezomib is most commonly given as a 20 second injection under the skin
or subcutaneously (SC) in the abdomen but can also be given into a vein or
intravenously (IV). Bortezomib can be given on a weekly schedule or twice
weekly schedule and for differing lengths of time. The specialist will advise how
often bortezomib is required and for how long in each individual case.

Bortezomib is often given in combination with dexamethasone and cyclophos-
phamide, known by the acronym CyBorD or VCD. For a list of these combinations,
see Table 4.
Although people do not normally need to be admitted to hospital to have treatment with bortezomib, they do have to travel to the hospital regularly to receive bortezomib in the day chemotherapy unit.

**What are the potential side effects of bortezomib?**

In general the side effects of bortezomib are mild to moderate, however this can vary. It is important to highlight side effects promptly to the doctor or nurse. The most common side effects are:

- Lowered white cell count (Neutropenia)
- Lowered platelet count (Thrombocytopenia)
- Gastrointestinal problems; nausea, vomiting, diarrhoea and constipation
- Peripheral neuropathy
- Low blood pressure; feeling dizzy or faint, especially when standing too quickly
- Increased risk of a shingles infection

Drinking plenty of water on the days of treatment can reduce the risk of some of these effects. Blood tests will be taken at regular intervals during therapy to watch for the effects of toxicity or lowered platelet counts. If signs of peripheral neuropathy develop inform a doctor or nurse.

See Table 3 for a more details of each side effect. It is important to inform the doctor if any side effects are experienced.

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See our Bortezomib Treatment Fact Sheet for more information.

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**Carfilzomib (Kryprolis®)**

Carfilzomib is a relatively new proteasome inhibitor that targets a different part of the proteasome to bortezomib. Carfilzomib is administered intravenously (IV) over 30 minutes or less and is given on 2 consecutive days per week for 3 weeks followed by 1 week break. It can be given on its own (monotherapy) or in combination, usually with steroids. It has a lower risk of neuropathy than bortezomib. In some studies small numbers of people given carfilzomib
experienced problems associated with high blood pressure, shortness of breath, kidney impairment or reduced heart functioning. Careful monitoring is required for those receiving carfilzomib who have preexisting blood pressure problems or heart conditions.

What are the potential side effects of Carfilzomib?

- Lowered red cell count (anaemia)
- Lowered platelet count (thrombocytopenia)
- Gastrointestinal problems; nausea and diarrhoea
- Fatigue
- Shortness of breath
- Increased blood pressure
- Changes in kidney function tests

Drinking plenty of water on the days of treatment can reduce the risk of some of these effects. Some patients may require IV hydration in advance of their dose of carfilzomib, particularly during the 1st cycle of therapy. Blood tests will be taken at regular intervals during therapy to monitor the blood counts and potential side effects.

See our Carfilzomib Treatment Fact Sheet for more information.

www.myeloma.org.au – 1800 MYELOMA (693 566)

Ixazomib (Ninlaro)

Ixazomib is also a proteasome inhibitor and is given in combination with steroids such as dexamethasone or prednisolone. Ixazomib is a tablet, given once per week for 3 weeks followed by a week's break. Clinical studies have shown ixazomib to be well tolerated with the more common side effects being lowered blood counts, gastrointestinal effects such as diarrhoea or constipation, and a low risk of peripheral neuropathy.

Ixazomib may be available in Australia within clinical trials and through patient access schemes. Ask the treating doctor more about their suitability in each individual case.
Monoclonal Antibody Drugs (MoAbs)

Monoclonal antibodies are a class of drug that have been widely used to treat other types of cancers but only recently are being used in myeloma. They work by recognising specific proteins on the cancer cell surface and attaching to them. This then alerts the body’s immune system to attack.

There are a range of MoAbs being investigated for use in myeloma. Two of the more promising ones are daratumumab (Darzalex®) and elotuzumab (Empliciti®). Daratumumab is designed to attach to the CD38 protein. It is given intravenously and can be effective on its own or in combination with other drugs. Elotuzumab is also given intravenously and is designed to attach to the SLAMF-7 protein. It has shown to be more effective when used in combination with other drugs such as the IMiDs, rather than on its own.

What are the potential side effects of MoAbs?

Pleasingly, the side effects associated with the MoAbs seem quite minimal. There is a risk of an allergic like reaction which tends to occur most commonly with the first dose. Symptoms of allergic like reactions include fever, chills, cough, rash and difficulty breathing. Medications to prevent these symptoms are given prior to the infusion.

Other possible side effects are:

- Nausea
- Diarrhoea
- Fatigue
- Lowered red cell count (anaemia)
- Lowered platelet count (thrombocytopenia)
- Lowered white cell count (neutropenia)

See Table 3 for more details of each side effect. It is important to inform the doctor if any side effects are experienced.
At the time of publishing both these drugs are not available on the PBS but may be accessible via clinical trial or compassionate access schemes. Ask the treating doctor about these drugs and their current availability.

See our Daratumumab Treatment Fact Sheet for more information.

www.myeloma.org.au – 1800 MYELOMA (693 566)

Table 3 – Potential Side Effects of Myeloma Treatment

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Sleepiness  | • Thalidomide is a known sedative and therefore should be taken in the evening  
• Take thalidomide a few hours before bedtime if it is hard to rise in the morning |
| Constipation| • Maintain a high fibre diet with plenty of fluid. Aim to drink 2.5 - 3 litres of fluid a day  
• Regular exercise as tolerated  
• Use of laxatives is commonly required |
| Rash        | • If occurs, is likely to happen within the first few doses  
• Inform the doctor if a rash appears  
• Likely to improve on its own  
• May require stopping the drug if severe |
| **Peripheral neuropathy** (tingling, burning, pain, and loss of feeling in hands and feet) | • More common with high doses and after taking thalidomide or bortezomib over longer periods of time. Less common with lenalidomide.  
  • Inform the specialist if symptoms of neuropathy appear  
  • May require a dose reduction  
  • **See Myeloma Australia’s Managing peripheral neuropathy booklet for a comprehensive list of suggestions to help reduce the impact of peripheral neuropathy.** |
|---|---|
| **Thrombosis – Risk of developing blood clots** | • More common if other risk factors are present such as obesity, older age, high myeloma protein and previous history of heart disease or stroke  
  • Often requires the taking of a blood thinning medication such as aspirin, warfarin or low molecular weight heparin to reduce the risk of blood clots  
  • Symptoms of a DVT include swelling, redness, warmth and tenderness in the leg  
  • Symptoms of a PE include shortness of breath and chest pain  
  • Inform the doctor at once if symptoms of a blood clot occur. |
| **DVT – deep vein thromboses (commonly in the lower leg)** |  |
| **PE – pulmonary emboli (clot in the vessels of the lungs)** |  |
| **Thrombocytopenia: low levels of platelets** | • If platelets become very low, there is an increased risk of bleeding. The doctor may recommend a platelet transfusion  
  • Bruising can be a sign of lowered platelet count |
**Neutropenia: low levels of neutrophils, a type of white blood cell**

- Regular blood tests are used to check cell counts during treatment
- If the number of these cells is very low, the doctor may change the dose and/or schedule of the treatment
- Be aware of the signs and symptoms of infection such as a temperature above 38ºC, having a productive cough, experiencing shivers or chills, swelling or redness at site of a cut or injury
- Report any signs of infection to the GP or specialist

**Gastrointestinal Problems: nausea, vomiting, diarrhoea, and constipation**

- Keep well hydrated (2.5 - 3 litres fluid a day).
- Take anti sickness medication as prescribed

**For diarrhoea:**
- The BRAT diet may help (bananas, rice, apple sauce, toast)
- Take antidiarrhoeal medication as prescribed (e.g. loperamide)

**For constipation:**
- High fibre foods
- Keep well hydrated
- Take laxatives as required
| Low blood pressure; feeling dizzy or faint, especially when standing up too quickly | • If also taking drugs that lower blood pressure, medications might need to be adjusted  
• Drink plenty of fluids especially on the days when having treatment. If insufficient liquids are taken the doctor may need to administer some intravenous fluids prior to therapy if attending a clinic. |
| --- | --- |
| Fatigue | • Fatigue can be a symptom of myeloma and a side effect of treatment.  
• See page 57 for more information on fatigue |

See our fact sheets for more information on medications to treat myeloma and how to manage side effects.  

www.myeloma.org.au - 1800 MYELOMA (693 566)
Combinations of treatments

Although sometimes a drug is used on its own to treat myeloma, more commonly combinations of drugs are used. The following section explores some of the different common combinations used and the rationale for their use.

Initial therapy combinations for people eligible for high dose therapy and stem cell rescue (induction therapy)

Those suitable for this approach to initial treatment would include those who are younger and fitter. Most commonly this would be those under 70yrs of age but increasingly it is the general health of the person that is considered and not just the individual’s age. This treatment approach is generally considered more aggressive and toxic and can cause unacceptable side effects in older, less fit individuals. The risk of any treatment choice needs to be balanced against the likely benefits.

The aim of initial therapy is to gain control over the myeloma and reduce its effects on the body. Typically, this will involve 3 to 6 cycles of therapy with a cycle being 3 to 4 weeks in length (total treatment of 3-6months).

The most common treatment regimens (protocols) used when a transplant is planned are listed in Table 4. These combinations may include drugs of which some are given into a vein (intravenous, IV), under the skin (subcutaneous, SC) and some are given orally. An acronym consisting of single letters is used for convenience. Each of the letters in these combinations represents a different drug, e.g. in the case of CVD they are Cyclophosphamide, Velcade and Dexamethasone.

Initial therapy combinations for people not eligible for high dose therapy and stem cell rescue (induction therapy)

If a transplant is not planned then similar combinations of therapy are recommended. These include boretzomib, lenalidomide or thalidomide based treatment. When deciding on the best treatment in this group of individuals, considerations of an older, and potentially less fit person are taken into account. Frailty and presence of pre-existing health issues can be more common and the ability to tolerate combination therapies and frequency of hospital visits need to be taken into account when deciding on best treatment for any individual.
Disclaimer

Due to the pace of change in the treatment of myeloma it is beyond the scope of this guide to list optimum combinations of treatment for each phase of the disease and in any particular individual. We have chosen therefore, to present a table of the most common combinations. For more specific information about which treatment combination is most suitable for an individual, ask the specialist.

Newer drug combinations are often available first as part of organised clinical trials. Ask the specialist for more information about this option.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Drugs included</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy based combinations</strong></td>
<td></td>
</tr>
</tbody>
</table>
| CD           | Cyclophosphamide  
              | Dexamethasone  |
| DPACE        | Dexamethasone  
              | Cisplatin  
              | Doxorubicin  
              | Cyclophosphamide  
              | Etoposide  |
| MP           | Melphalan  
              | Prednisolone  |
| **Bortezomib (Velcade®) based combinations** | |
| VD           | Bortezomib  
              | Dexamethasone  |
| CyBorD (also known as VCD) | Cyclophosphamide  
              | Bortezomib  
              | Dexamethasone  |
| VMP          | Bortezomib  
              | Melphalan  
              | Prednisolone  |
| **Carfilzomib (Kyprolis®) based combinations** | |
| KD           | Carfilzomib  
              | Dexamethasone  |
### Thalidomide (Thalomid®) based combinations

| TD   | Thalidomide  
|      | Dexamethasone |
| CTD  | Cyclophosphamide  
|      | Thalidomide  
|      | Dexamethasone |
| MPT  | Melphalan  
|      | Prednisolone  
|      | Thalidomide |

### Lenalidomide (Revlimid®) based combinations

| RD   | Lenalidomide  
|      | Dexamethasone |
| RCD  | Lenalidomide  
|      | Cyclophosphamide  
|      | Dexamethasone |

### Pomalidomide (Pomalyst®) based combinations

| PD   | Pomalidomide  
|      | Dexamethasone |

### Disclaimer

New drugs are being approved for reimbursement through the PBS each year in Australia. Drugs are approved for a specific indication which determines who with myeloma can access them, in combination with what other drugs and at what stage of their treatment pathway. The haematologist will recommend the most effective regime available in each circumstance.

Ask the nurse and specialist for further information on a particular treatment regimen, including advantages, disadvantages and potential side effects.
High Dose Therapy and Autologous Stem Cell Transplantation (AuSCT)

What is high dose therapy and stem cell transplantation and why is it needed?

Standard chemotherapy, given alone or in combination, is an effective way of treating myeloma. In the majority of cases chemotherapy is easy to administer and can often be taken at home. However, a major drawback of chemotherapy is the inability to give high doses safely. This is because chemotherapy, particularly in higher doses, kills healthy, good cells as well as myeloma cells. This can result in blood production being severely affected and blood cells may fall to dangerously low levels, causing a number of potentially serious problems such as neutropenia and thrombocytopenia.

An autologous stem cell transplant uses healthy cells, previously collected from the patient’s blood, to offer a way round the problem. It provides a means of giving higher doses of chemotherapy, to consolidate previous chemotherapy treatment, without causing permanent damage to blood cell production.

Giving back previously collected healthy stem cells after high dose chemotherapy effectively ‘rescues’ the patient’s bone marrow. It means that healthy blood cell production can continue until the bone marrow, damaged by the high doses of chemotherapy, recovers and produces new cells.

High dose therapy and stem cell transplantation therefore has the ability to destroy in a safe way more myeloma cells than would be possible with lower doses of chemotherapy, improve the duration of remission and provide better quality of life.

It is worth noting however, that myeloma is a very individual disease. Each person’s myeloma has its own distinct characteristics, which may affect the outcome of high dose therapy and stem cell transplantation and not all people achieve the desired response.

For a small group of younger people, an allogeneic transplant may be used after an autologous stem cell transplantation. Allogeneic transplantation is discussed later in this guide.
What are blood stem cells?

Blood forming stem cells exist in the bone marrow. They have the capacity to divide and develop into the three main types of cells found in the blood and are a vital component of high dose therapy and stem cell transplantation (see Figure 4).

Figure 4. Blood stem cell diagram
High dose therapy and stem cell transplantation – the process

The whole process, from the initial discussion with the doctor to recovery after the transplant, can take several months and can be daunting if approached as a whole. It is often easier to prepare for and face each stage separately.

Due to the nature of this treatment option, only hospitals with appropriate accreditation and medical and nursing experience perform high dose therapy and stem cell transplantation. This may mean a referral to another hospital for this portion of treatment and care.

Induction chemotherapy / treatment

The combinations of treatments discussed in the previous chapter are required before high dose therapy and stem cell transplantation can take place. This initial treatment, known as induction therapy, aims to reduce the amount of myeloma in the body and help relieve the symptoms. There are a number of induction regimens to choose from, all of which have been shown to be comparably effective. Individual disease factors as well as doctor / patient preference will determine which regimen is the most appropriate to use.

Courses of induction therapy usually last for several months and are given in cycles. The number of cycles given will depend on individual factors and how the myeloma responds, however 3 to 6 months would be a common duration of therapy.

How are stem cells collected – ‘Mobilisation’

Stem cells that are collected from blood are referred to as peripheral blood stem cells or ‘PBSC’. These stem cells live and grow in the bone marrow. It is necessary then to move the stem cells into the blood stream in order to be able to collect them.

This is achieved by giving a special type of drug called a ‘growth factor’. Growth factors are then given daily to increase the number of stem cells in the bone marrow, causing them to spill over into the blood where they can be collected more easily. The growth factors are given consecutively over about 7 to 10 days before there are enough stem cells to be collected. Some centres may also use a dose of chemotherapy at the beginning to kill off a population of mature blood cells causing new cells to grow in their place. The administration
of the chemotherapy may require a few days in hospital but the remainder of the mobilisation process can be carried out as an outpatient.

Once the stem cell count is high enough, collection will take place using a special machine known as a cell separator or apheresis machine. This process is carried out in the day care area of the hospital. Collecting the stem cells usually takes about 3 to 4 hours lying down on a bed or special lounge chair with a line connected into a vein in each arm.

Blood is taken from one arm and goes through the line, into the apheresis machine. The blood is centrifuged to separate the various cell components. Stem cells are drawn off and the remaining blood returned through the intravenous line into the other arm. During the stem cell collection process, the most common side effect is a cramp like or tingling sensation in the hands, feet or around the mouth. This happens because an anti coagulant agent is used to stop the blood from clotting in the machine and this can cause a drop in the body’s calcium levels. This is usually easily corrected by drinking some milk. It is normal to feel tired after the collection and need to rest that evening.

Often, enough cells will be collected in just one session but sometimes another session the following day is required to collect enough stem cells to transplant.

**Receiving the high dose chemotherapy**

After the stem cells have been frozen and stored, the next step is to come into hospital to receive the high dose chemotherapy followed by the transplant of stem cells. There is usually a gap of about a month between the collection of stem cells and the receiving of high dose chemotherapy.

Although it can vary between patients, this part of the process usually requires a 3 to 4 week stay in hospital. Some transplant centres carry out this process as a mixture of inpatient and outpatient care. Ask the specialist or nurse to explain these details.

The high dose chemotherapy is often referred to as ‘conditioning’ therapy and is given through a vein, usually via a central line (e.g. Hickman® catheter or a PICC line).

The insertion of the central line involves a small procedure to have a narrow plastic central line inserted into a large vein in the upper chest. This form of central line allows all of the chemotherapy to be given without inserting a new
line into a vein at each visit. Blood samples can also be taken through this line. The PICC line is similar, but inserted in the arm. See diagram Figure 5.

The high dose chemotherapy is called melphalan, an effective drug in treating myeloma. Before and after melphalan is given, large amounts of fluid are given through a drip, to prevent dehydration and kidney damage caused by the toxicity of the chemotherapy.

The most common side effect of melphalan is nausea and gastric upset, commonly diarrhoea. These symptoms can be ongoing for 7 to 10 days but a range of medications will be given to minimise these side effects. Any side effects should resolve as the blood counts improve.

Within a day or so of completing the high dose melphalan, the frozen stem cells are thawed and given back as an intravenous drip. This process is relatively straightforward and takes roughly 15 minutes per bag of stem cells.
**Engraftment**

Once the stem cells are put back into the blood stream, they settle in the bone marrow and develop into new blood forming cells – a process known as engraftment. This takes on average 10-14 days. Once blood cell numbers have returned to within safe levels and there are no signs of infection or other health issues requiring treatment, it is safe to go home.

During the crucial time waiting for engraftment there will be an increased risk of infections and the team will advise ways to minimise this. This will include a range of supportive medications like antibiotics and other anti microbials. It is important to maintain good hygiene with daily showers and changes of clothes. The mouth is a common route for infection so maintaining good oral hygiene is also important. One of the side effects of the chemotherapy can be a sore, dry mouth and a variety of cleaning or soothing agents may be recommended by the nursing team. There is some evidence to show that sucking ice for 30 minutes before the melphalan infusion, during and for 2 hours after the melphalan has finished, can reduce the severity of a sore mouth (mucositis). This is called ‘cryotherapy’ and seems to work by cooling the mouth and preventing damage to the lining of the mouth caused by the melphalan. Ask the nurse or doctor if this technique is appropriate.

Even though the appetite may be suppressed it is important to maintain a ‘clean diet’ to avoid the chance of picking up a gastric infection. This involves fresh cooked food, no raw meat or fish or unpasteurised dairy foods. Ask the dietician for more information on a clean diet. Fatigue is common during the process of engraftment, as is lack of concentration. This will improve over time but can often take months to recover to the pre transplant state.

**Supportive care and follow up when at home**

The recovery time at home after a transplant can be a challenging one. Energy levels often take months to return to normal and there will be regular specialist visits to check the blood cell numbers are returning to normal.

There will still be a risk of infections therefore it is important to maintain good hygiene, avoid people with infections and inform the doctor of signs and symptoms of infection, promptly. There will be a range of medications to protect the body from infections and 6 to 12 months after transplant some repeat
vaccinations will be required to regain childhood immunity that may have been lost. See the risk of infection section in this book for more information.

**What are the types of transplant that are available?**

If stem cells from oneself are used for the transplant, it is called an autologous transplant; if stem cells from a donor are used, it is called an allogeneic transplant. It is very important to understand that there are significant differences between these two types of transplant, both in their potential benefits and the risks involved.

**Autologous transplantation (AuSCT)**

Autologous transplants use stem cells collected from the patient (auto = self). This is the most common form of transplantation used in myeloma. In this kind of transplant, bone marrow recovery takes about two weeks. Blood and platelet transfusions may be required until the bone marrow recovers and antibiotics are usually given to prevent infections.

The main advantage is the possibility of achieving an excellent response and long remission with a low level of risk from the treatment. Disadvantages include more toxicity than standard dose chemotherapy and the reality that relapses still occur.

**Allogeneic stem cell transplantation (AlloSCT)**

Allogeneic transplantation (allo – from the Greek word meaning ‘other’) involves collecting stem cells from either the bone marrow or peripheral blood of another person (the donor) and giving them to the patient (recipient).

Because myeloma effectively ‘shuts off’ a vital part of the immune system that would normally kill myeloma cells, allogeneic transplants aim to use the immune system from the donated cells to help directly fight the myeloma in the patient (recipient).

The goal is for the donated cells to eventually replace the immune system of the patient and therefore continue to fight off the myeloma.

A transplant of stem cells from a donor has two main advantages: the transplanted cells do not contain any myeloma cells (no contamination), and the donor’s immune system has the ability to recognise and destroy myeloma cells.
The disadvantage of using a donor is that the donor’s immune cells will recognise the patient as ‘foreign’, and this can trigger a serious complication called **graft versus host disease** (GvHD). This is an adverse reaction that can affect the skin, liver and gut, causing serious problems, which may even be fatal.

In those patients who cope with the transplant and the complications, a number may have no detectable myeloma and potentially achieve a longer remission.

Even if the myeloma does recur, the transfusion of more of the donor’s immune cells, collected from their blood, can help to destroy the myeloma cells again. This procedure is called a donor lymphocyte infusion, or DLI.

If a patient does not have a brother or sister with the same tissue type as the patient, it is sometimes possible to find a donor who is not related. This type of transplant is called a matched / volunteer unrelated donor (or M / VUD) transplant.

The problems associated with this form of transplant are even greater than with a related donor. These transplants are very rare, they do happen but not enough to show what the long term benefit may be.

In order to reduce the risks associated with an allogeneic transplant, while still maintaining the benefits of giving donor cells, a newer type of transplant has been developed. This is the **reduced intensity conditioning** transplant (RIC) or the **mini allogeneic transplant**, which involves giving a lower dose of chemotherapy than would be used for a standard allogeneic transplant. For patients suitable for an allogeneic transplant, it is now common for their doctors to recommend a standard AuSCT followed by a reduced intensity allograft.

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See our Stem Cell Transplant – a guide for people with myeloma book for more information.

**www.myeloma.org.au – 1800 MYELOMA (693 566)**

For information about finding an allogeneic donor, visit the Australian Bone Marrow Donor Registry at **www.abmdr.org.au**
Maintenance treatment

After autologous stem cell transplant has brought the myeloma under control, maintenance treatment may be recommended to prolong the period of response to treatment, whether in remission or plateau. Maintenance treatments may be given as a combination or as a single agent. At the time of publication, thalidomide and lenalidomide are each approved and reimbursed for maintenance therapy in Australia after transplant.

It is important to know that not all people will benefit from maintenance therapy and any benefits will have to be balanced against the side effects that may occur. This should be discussed with the treating doctor. In addition, other myeloma treatments are being studied in clinical trials as potential maintenance treatments.
What are the treatments for symptoms and complications due to myeloma?

Supportive Therapy

Myeloma can affect the body in several ways. This is due both to the activity of the myeloma cells and to the release of a variety of proteins and other chemicals into the local bone marrow microenvironment and directly into the blood stream.

It is important to remember that not everyone will experience all of these and that treatments are available.

The most common symptoms and complications of myeloma, how they affect the patient, and how they are managed, are described below.

Bone disease

Bone disease is one of the most common complications of myeloma. The myeloma cells release chemicals that activate osteoclast cells, which destroy bone, and block osteoblast cells, which normally repair damaged bone.

When this happens, the bone is broken down faster than it can be repaired, leading to bone pain, bone lesions or even fractures. The middle or lower back, the rib cage and the hips are the most frequently affected areas. Fractures occur most often in the spine (vertebrae) or ribs. Fractures can sometimes occur with only minor pressure or injury. Fractures of the vertebrae can lead to their collapse causing pain due to trapped nerves, loss of height and curvature of the spine. The rapid breakdown of bone can lead to an increase in the blood calcium level (hypercalcaemia) which can cause symptoms of confusion, constipation and thirst.

A group of drugs called bisphosphonates are used to help manage myeloma bone disease.

Bisphosphonates help in myeloma in several ways. They help to correct hypercalcaemia, control existing bone disease, and slow down any further bone destruction. They work by binding to calcium in the bone and by blocking the activity of the osteoclast cells that break down the bone.

Evidence from clinical studies with bisphosphonates has shown that there is a benefit to be gained by giving bisphosphonates to any patient with active myeloma, whether they have symptoms of bone disease or not.
In Australia, three bisphosphonates are currently licensed for the treatment of hypercalcaemia and / or bone disease in myeloma. They are:

- Zoledronic acid (Zometa®), which is given as an intravenous infusion
- Pamidronate (Aredia®), which is given as an intravenous infusion
- Sodium Clodronate (Bonefos®), which is taken by mouth as tablets

There is also a type of monoclonal antibody treatment that can improve bone strength, denosumab (Xgeva®). It works by preventing the chemicals produced by the myeloma cells that upset the healthy balance of bone formation.

It is given as a sub-cutaneous injection (into the skin) once per month and is safe for people with kidney impairment.

Denosumab is commonly used in the treatment of osteoporosis and in people with bone metastasis in other cancers. Its use in myeloma is still under investigation and not reimbursed by the Pharmaceutical Benefits Scheme as yet. Some people may be able to access denosumab under special circumstances as directed by their doctor.

**Osteonecrosis of the Jaw – ONJ**

A complication associated with bisphosphonate therapy is a condition called osteonecrosis of the jaw (ONJ). It is seen in a small number of people receiving bisphosphonate therapy. ONJ presents as a persistent non healing wound in the mouth most commonly following tooth extraction or dental surgery. It can cause pain, may become infected and is slow to heal.

It is important to note that bisphosphonate therapy is an important part of the supportive care of those with myeloma. Bisphosphonates reduce the risk of further bone disease, bone pain and high calcium levels in the blood. The low risk of developing this rare complication needs to be balanced with the obvious proven benefits of these drugs.

**Who is at greater risk of getting ONJ?**

The risk of developing ONJ in those with myeloma is thought to be less than 10% overall. Some factors are known that increase the risk of developing ONJ:

- Prolonged use of bisphosphonates (> 12months)
- Undergoing invasive dental procedures such as tooth extraction or surgery exposing jaw bone
• Those with poor dental health
• Smoking
• Those with diabetes
• Having poorly fitting oral appliances (e.g. dentures)

How to prevent ONJ?
Avoiding the risk factors above can minimise the risk of developing ONJ. It is also recommended that everyone has a thorough dental check before they start treatment with bisphosphonates and undertake any invasive dental work before they commence therapy. Six monthly dental assessments should occur during therapy. The dentist should be informed if patients are receiving bisphosphonate treatment.

If a tooth extraction or dental surgery is required whilst on bisphosphonate therapy, ask the dentist and specialist to have a discussion in advance to decide on the best treatment. It is often advised to have a break from bisphosphonate therapy whilst extraction or surgery is undertaken and until complete healing has occurred. A course of antibiotics may also be required and maintaining impeccable oral hygiene is essential.

How to manage ONJ should it occur?
Therapy to manage ONJ, should it occur, is conservative and will depend on individual risk factors, such as bone disease or whether the myeloma is stable or in remission. The following gives some guidance as to the management of ONJ but concerns can be discussed with the specialist and dentist.

• Pain control
• Antibiotics
• Regular mouth washes – chlorhexidine 0.2%
• Regular dental review
• A ‘drug holiday’ from bisphosphonate therapy

It is now recommended that the use of bisphosphonates be assessed every 12 months. A decision to continue or modify bisphosphonate therapy should be made based on the risk of a skeletal injury.
Pain

Pain is the most common symptom for people with myeloma and is often related to underlying bone disease. Effective management of pain and its relationship to quality of life is critical and just as important as the treatment for the actual myeloma.

Pain is very specific to the individual and treatment will vary. Medication should aim to provide continuous pain relief whenever possible with a minimum of drug related side effects.

Complementary therapies such as relaxation techniques, aromatherapy and hypnosis have also shown to have some benefit for individual patients.

In some more serious cases medication and/or complementary therapies will need to be supplemented by other types of treatment such as:

- **Localised radiotherapy**: This has been shown to help control ‘hot spots’ of active bone disease and pain.

- **Vertebroplasty**: Vertebral collapse in the spine can often occur with myeloma. Vertebroplasty is a procedure which involves the injection of cement into the affected vertebrae body by a specialist radiologist. This procedure can significantly reduce pain.

Fatigue

Fatigue is well recognised in those with myeloma. It is described as a physical, emotional and/or cognitive tiredness or exhaustion related to myeloma or its treatment, which interferes with usual functioning.
The most important part of treating fatigue is actually recognising it. This means describing these feelings to the doctor.

Fatigue is often described as a vicious cycle, but the cycle can be broken, allowing it to be managed. Planning activities to avoid becoming overtired is something both patient and carers can do together. Other strategies to help reduce fatigue include eating a healthy, balanced diet, taking regular light exercise and ensuring adequate sleep.

Fatigue caused by anaemia can be treated with blood transfusions and in certain cases also with a drug called erythropoietin. See also the section on anaemia below.

Kidney damage

Kidney problems can occur in myeloma for a variety of reasons. The abnormal protein produced by myeloma cells can damage the kidneys; this is particularly common with the Bence Jones protein. Other complications of myeloma, such as dehydration and hypercalcaemia, as well as some of the drugs used to treat myeloma and its complications can also cause kidney damage.

The most important method to reduce the risk of kidney damage is to drink plenty of fluid. Drinking 3 litres of fluid per day is optimal. This includes all fluids from tea and coffee, fruit juice, milk and water. Some people find it useful to keep a bottle of water with them at all times so they always have a drink to hand.

Avoid using a certain type of painkillers called a non steroidal anti inflammatory drug ‘NSAIDs’ such as naprosyn or ibuprofen (Nurofen®). These drugs may contribute to kidney problems. The ‘contrast dye’ given during certain types of scans (including CT scans) can also harm the kidney and should be avoided if possible.

Treatment of kidney damage in myeloma depends on the cause. In many cases, the kidney damage is temporary and your kidneys can recover. In a small proportion of patients, the kidney problems become permanent.
requiring a regular treatment called kidney dialysis. This is a way of filtering the blood using a dialysis machine in the same way that kidneys would do if they were healthy.

**Anaemia and infections**

In adults, almost all red blood cells, white blood cells and platelets are made in the bone marrow. Red blood cells contain a protein called haemoglobin, which carries oxygen around the body. White blood cells help the body fight infection. Platelets are small cells that circulate in the blood, and are important for helping the blood to clot.

Myeloma cells crowd out normal cells in the bone marrow and create conditions that favour themselves, so fewer blood cells are produced. This shortage of blood cells can lead to conditions such as anaemia or to more frequent infections.

Table 5 – Complications of reduced blood cells:

<table>
<thead>
<tr>
<th>Anaemia</th>
<th>Too few red blood cells result in a low haemoglobin level. This leads to tiredness and weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>Low levels of white blood cells, in particular the neutrophils, can make infections more likely</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Low levels of platelets may cause bruising or bleeding</td>
</tr>
</tbody>
</table>

Anaemia is a reduction in the number of red blood cells or the oxygen carrying haemoglobin they contain. It can occur as a result of the myeloma or as a side effect of treatment and can cause symptoms of fatigue and weakness.

Anaemia does not always need treatment because the bone marrow is often able to recover, especially if treatment brings the myeloma under control.

If anaemia needs treatment, a blood transfusion can help, there is also a drug called erythropoietin (or EPO) which can stimulate the body to produce more red blood cells. In Australia, EPO is available to those who have kidney damage.
If the platelet count falls to very low levels, it can be boosted by a transfusion of platelets.

**Risk of infection**

Low white cell counts may not always need to be treated, but symptoms of infection should be taken seriously (such as fever, coughing up green phlegm, pain in passing urine, or diarrhoea) by notifying a doctor straight away. It is useful for patients to keep a thermometer at home to take their temperature if feeling unwell. **If the temperature display is equal to or greater than 38°C a doctor should be informed immediately.**

If the white cell count falls very low, the doctor may prescribe a course of antibiotics to try to prevent infections before they take hold. There are also drugs (called growth factors) that can stimulate the body to produce more white blood cells.

Having an annual flu vaccination is generally recommended for people with myeloma and those living in the same household. This would not be recommended if the immune system was very low or someone had an active infection. Check with the specialist or GP to see if the flu vaccination would be beneficial.

**Key Points**

- Be honest about any problems. Describing them as accurately as possible will help get the right treatment.
- Acting early can reduce the number and severity of the complications associated with myeloma.
- Bone disease can be treated effectively with bisphosphonates, and early treatment can slow down bone problems.
- Drink plenty of water / fluids to prevent kidney problems – aim for 3 litres per day.
- If buying painkillers, tell the pharmacist to avoid nonsteroidal anti inflammatory drugs.
- Tell the doctor or nurse immediately if there is any concern about an infection.
For more comprehensive information on the risk of infection, bone disease, pain, fatigue and more, see our Living Well with Myeloma book and fact sheets 1800 MYELOMA (693 566) - www.myeloma.org.au
How is myeloma treated when it becomes active again?

Treatment for relapsed or resistant myeloma

When myeloma returns, it is called a relapse or disease progression. This can be a very disappointing and distressing time for people living with myeloma, their families and carers. Talking things over with the doctor, family / carer or another person living with myeloma can help. Myeloma Australia or one of the organisations listed at the back of this guide are other good sources of support and information.

When myeloma returns, patient and doctor will consider which treatment will be needed to try to regain control of the disease. This may already have been discussed in the initial treatment plan. However, because the risks and benefits of treatment are not as clear in people whose myeloma has relapsed, many doctors like to discuss all the options again, as views and the disease characteristics may have changed.

In some patients, the original treatment can be repeated successfully, especially if the initial response to treatment was good. In other patients, the myeloma may not respond to the treatment that was used previously; this is called resistant or refractory disease.

If the myeloma is resistant / refractory to the original therapy, there are still many options available.

These include:

- Thalidomide (Thalomid®) based combination
- Bortezomib (Velcade®) based combination
- Lenalidomide (Revlimid®) based combination
- Pomalidomide (Pomalyst®) based combination
- Carfilzomib (Kyprolis®) based combination
- Trying a different type of chemotherapy combination
- Undergoing another high dose therapy and stem cell transplantation
- One of several newer agents not yet freely available in Australia but available within clinical trials or via compassionate access schemes.
Trying a different type of chemotherapy

If the myeloma is no longer responding (refractory) to one type of chemotherapy such as melphalan, a patient may respond to more intensive combinations such as DT-PACE (Dexamethasone, Thalidomide, Cisplatin, Adriamycin, Cyclophosphamide, Etoposide). These regimes may be an option in younger patients to regain disease control so that high dose therapy and stem cell transplantation may still take place.

Having a second high dose therapy and stem cell transplantation (AuSCT)

For some people, a second transplant procedure may be an effective strategy, especially if they have had a good response to the first transplant and are in good health.

In people who have not had a prior stem cell transplant, high dose therapy and stem cell transplantation may be considered.

Steroids

High dose therapy steroid treatment with dexamethasone can be effective in controlling myeloma for people who cannot have chemotherapy because of their general health, or who have relapsed more than once following chemotherapy.
How to know if the treatment has worked?

The aim of treatment is to control the disease and its effects on the body. In order to find out the response to treatment, several tests will be carried out on a regular basis.

These tests may vary, but generally include regular blood and urine testing, bone marrow sampling and occasional x-rays or scans.

The signs that treatment is working are a fall in the paraprotein level, less bone pain, improvement in anaemia and a reduction in the number of plasma cells in the bone marrow. However, one of the best indicators of response to treatment is an improvement in general health.

In general terms, disease response is measured and categorised in Table 6 Response Criteria. These criteria are defined using very specific standards, or criteria and are used in clinical trials to determine outcomes of treatments.

It is important to note once again that the duration of response is as important as the level of response.
Table 6 – Response Criteria
Outcomes based on criteria developed by the EBMT (European Group for Blood and Marrow Transplant) and IMWG (International Myeloma Working Group Uniform Response Criteria).

<table>
<thead>
<tr>
<th>Type of Response</th>
<th>Paraprotein</th>
<th>% Plasma Cells in the Bone Marrow</th>
<th>Skeletal Disease (on -x-ray)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stringent complete response (sCR)</strong></td>
<td>No longer detectable in the blood and/or urine; negative immunofixation test; normal free light chain ratio</td>
<td>&lt;5%; no myeloma cells present</td>
<td>Stable</td>
</tr>
<tr>
<td><strong>Complete response (CR)</strong></td>
<td>No longer detectable in the blood +/- urine; negative immunofixation test</td>
<td>&lt;5%</td>
<td>Stable</td>
</tr>
<tr>
<td><strong>Very good partial response (VGPR)</strong></td>
<td>No longer detectable in the blood +/- urine, but positive immunofixation test, or 90% decrease</td>
<td>N/A</td>
<td>Stable</td>
</tr>
<tr>
<td><strong>Partial response (PR)</strong></td>
<td>≥50% decrease</td>
<td>N/A</td>
<td>Stable</td>
</tr>
</tbody>
</table>
**Minimal Residual Disease (MRD)**

Minimal residual disease is the name given to any remaining (residual) signs of myeloma following treatment that is not routinely visible through conventional measures and tests. It is increasingly thought that being able to assess MRD is key to predicting relapse in any individual and in time, will help direct more individual treatment plans. Methods being used to assess for MRD include specific genetic tests and improved scanning techniques.

To read more about MRD see International Myeloma Foundation Black Swan Research Initiative at [www.myeloma.org](http://www.myeloma.org)
New treatments and clinical studies

There are many research projects looking to find more effective and less toxic treatments for myeloma. Many new treatments are in development and some of the most promising drugs are mentioned here.

However, until the effectiveness and safety of these treatments has been established, they are generally only considered for patients whose disease has progressed or returned after more established treatments.

The best and safest way to take any new drug or treatment is as part of an approved clinical study. It is important to understand that not every patient is suitable for every new treatment but if patients are interested in trying a new treatment, this should be discussed with their doctor or nurse.

Clinical studies are planned investigations, involving patients, designed to test new treatments or to compare different types of current treatment. They are run according to a strict set of guidelines called a protocol.

All patients involved in a study are closely monitored. The information collected during the course of the study is combined and analysed by trained researchers. The results will help to determine which are the best treatments and the most appropriate doses, to help improve care for patients in the future.

Being asked to participate in a clinical study does not necessarily mean being asked to try a new treatment. The study may be testing new ways of using current treatments. In some hospitals, treating cancer patients in clinical studies is part of standard practice.

What are the different types and phases of clinical studies?

Preclinical studies

These are studies carried out in the laboratory testing new ways of killing myeloma cells. The next step is to understand if the treatment dose can be delivered safely to patients. The only way of achieving this is to give increasing doses to laboratory animals and observe for side effects.

Phase I

Researchers test a new treatment in a small group of patients for the first time to evaluate safety, dosage range and identify side effects. It is not the aim of the study to identify whether a treatment works or not.
Phase II
Larger studies to look at the size of the response obtained and efficacy compared with previous standard treatments.

Phase III
Larger studies than phase II. They are randomised and compare the best current standard treatment with the new treatment. The new treatment will have been shown to be effective in the phase II study and the effect will be at least as good as and sometimes better than the best current standard treatment.

Phase IV
Studies carried out after the treatment has been introduced into everyday use. They continue to test treatment to collect information about its effects in various groups of patients and any side effects associated with long term use.

As more is discovered about experimental treatments, their role alongside the more established treatments will become clearer. In time, if proved to be more effective and safer; they may replace some of the existing treatments. Because not all new treatments are better than standard treatments, it is important to carry out clinical studies to test these new treatments thoroughly.
What are some of the newer treatments being explored in myeloma?

New approaches include:

• Targeted treatments and monoclonal antibodies, which are intended to attack myeloma cells while leaving healthy cells alone.
• Vaccines, which try to boost the immune system’s ability to attack myeloma cells.
• Increasing the ability of the immune system to recognise and kill myeloma cells.
• Ways to disrupt the myeloma cells’ ability to divide.
• Ways of blocking messages within the bone marrow microenvironment that help to keep myeloma cells alive.

To find out more about clinical trials, what they are and what participation may involve, contact the Cancer Council to obtain a booklet or download directly from their website

www.cancercouncil.com.au

Alternatively, there is a range of information via Cancer Australia ‘Australian Cancer Trials’ www.australiancancertrials.gov.au

Or the Australian and New Zealand Clinical Trials Registry (ANZCTR) www.anzctr.org.au

Or for smart phone users search for ClinTrial Refer in the App Store for a frequently updated database of clinical trials in Haematology in Australia and New Zealand.
Living with myeloma

A diagnosis of myeloma affects everyone differently. At first it might be overwhelming, causing shock or a numb feeling. Information may not sink in at this point but don’t worry, there will be many opportunities to ask more questions.

Sometimes feelings may be controlled and at other times strong emotions may take hold. Some common reactions are fear, anger and frustration. These feelings are a natural part of coming to terms with the diagnosis. Learning more about myeloma, treatment options and life after myeloma treatment can help ease these feelings. It is also important to build good support networks for both patient and carer as effective communication can help to alleviate emotional stress.

Many patients experience depression and anxiety at some stage in their illness. It is not uncommon to feel optimistic at times and on other occasions to feel overwhelmed. Having difficulty sleeping, feeling irritable or experiencing a loss of interest in activities normally enjoyed, can be signs of increased anxiety or depression. It is important to recognise these symptoms and to discuss them with the doctor or nurse so that they can be managed effectively.

Emotional support

Emotional support is important for living with myeloma. It is very easy for patients and family members to feel isolated, and strong emotions often make it difficult to discuss worries or fears. Talking to someone who understands what is happening can ease these feelings of isolation.

Many people find that a specialist nurse is a good person to talk to. Contact the Myeloma Australia support line on the number below to talk to a myeloma support nurse in confidence. If finding emotions difficult to cope with, the doctor can make a referral to a counsellor or psychologist for help.

Support groups provide an informal and comfortable atmosphere in which members can share experiences and information. Many people assume that groups will be full of doom and gloom, but generally they are not. They are a supportive group of people who are facing the same things.

Some support groups are run by patients and family members, others by healthcare workers or professional group facilitators. If there is not a myeloma
group nearby, there may be a general cancer / haematology group that meets locally.

Call the Myeloma Australia Telephone Support Line, or ask the doctor or nurse if there is a myeloma support group nearby.

Family members can offer each other support by talking and listening. Being a good listener is an effective way to offer support and help ease anxiety of others. It is difficult to know how another person is feeling but trying to understand and empathising can help.

Counsellors offer the chance to explore feelings and experiences in a supportive, confidential environment. A counsellor does not give advice but helps find answers to the problems being faced.

Counselling may not always be available in the hospital but the specialist, nurse or GP will be able to recommend a professionally trained counsellor in the area. Alternatively the Australian Psychologists Referral Service can provide details of a local psychologist and can be contacted on 1800 333 497.

Myeloma Australia holds regular Seminars for people with myeloma and their family and friends; they provide a great opportunity to meet and share experiences with other patients and carers as well as a team of myeloma experts.

See our Living Well with Myeloma book for more on emotional health or for details of our Information and Support Groups and Seminars see 1800 MYELOMA (693 566) – www.myeloma.org.au

Allied health support

It is important to look after the whole body when living with myeloma and to seek the help of specialists when needed.

Podiatrist:

If peripheral neuropathy is an issue, seeing a podiatrist can ensure the feet are cared for and kept free from injury or infection.

Dietician:

If lack of appetite or taste changes are an issue, a dietitian can suggest strategies to maintain a balanced diet.
**Exercise physiologist or physiotherapist:**

If fatigue is an issue, an exercise physiologist or physiotherapist can be used to design an exercise program to help increase energy levels.

There are many more services available and some of these may be provided through the hospital. If not, the Medicare Australia Chronic Disease Management Plan entitles those living with myeloma to five allied health visits per year. Consult the GP for access to the plan and a full list of services available.

See our Living Well with Myeloma book for more on emotional health or for details of our Information and Support Groups and Seminars see 1800 MYELOMA (693 566) – www.myeloma.org.au
Communication with the medical team

Good communication with the medical team will involve a lot of trust and collaboration. There should be no hesitation in asking them questions or discussing treatment options. Learning more about myeloma and the pros and cons of different treatments will help to communicate more easily with them. Any treatment decision should be reached together.

Sometimes doctors and nurses use confusing medical language. If you do not understand something, please say so and ask for clarification. It is better that doctors and nurses explain it twice than to go home confused and worried.

Remember that the doctor may not be able to answer specific questions about the future. For example, predicting how successful a treatment will be. The doctor will probably be able to give average figures but these are not necessarily specific.

Tips:

• Take someone along to the appointments. This can help when recalling what has been discussed with your health practitioner.
• Ask if it is possible to record the consultation to play back later. Some hospitals may offer this service for you. Write questions down and give a copy to the doctor at the beginning of each consultation.
• Carry a piece of paper or notebook to write down questions as they arise.
• Always divulge any medications or complementary treatments, such as vitamin supplements, bought at the chemist or supermarket as some can interact with myeloma medications (e.g. high dose vitamin C and Green Tea should be avoided if taking bortezomib (Velcade®) therapy.)
• Tell the doctor about any symptoms or side effects.

Questions for the doctor / medical team

Diagnosis

• What tests are needed?
• When will results be available?
• Is treatment necessary?
• What is it likely to be?
• Are the bones affected?
• Are the kidneys affected?
• Who will be the main point of contact at the hospital from now on?
  (Write their details in this guide)

**Treatment**

• What are the treatment options?
• Is there a choice of treatment?
• What is the aim of this treatment?
• How successful has it been in the past?
• What would happen if treatment is delayed or denied?
• Is this treatment part of a clinical study?
• How experienced are you and your team in delivering this treatment?
• How is the treatment given, how long will it take?
• Will a hospital visit / stay be needed?
• What is it like before, during and after this treatment?
• Will there be side effects, when will they start and how long will they last?
• Will treatment affect the chance of having children in the future?
• What are the financial costs of this treatment?
• Will private health insurance cover the costs?

**Post treatment**

• How often are check ups and blood tests required?
• Are any other treatments e.g. bisphosphonates and maintenance treatments required?
• What are the signs that the myeloma has come back?

**Carers**

Carers often have different information needs. Carers will want to know what their roles and responsibilities may be.

• Will there be a stay in hospital and for how long?
• Will the person require a lot of looking after?
• What kind of quality of life is expected?
• Who can the carer call in an emergency?
Self help checklist

- Put aside time for relaxation
- Try to do one thing that brings enjoyment every day
- Recognise signs of stress or depression (feeling low, disturbed sleep, headaches, lack of appetite) and bring them to the attention of the doctor
- Learn about myeloma and its treatment – Many useful guides and websites are available
- Join a Information and Support Group; it can help to talk about feelings and experiences
- Use the Myeloma Australia Support Line: Toll Free 1800 MYELOMA (693 566)
- Find out from the GP, hospital doctor or nurse what services and benefits are available and ask for help if needed
- Ask if there is a social worker at the hospital who can help apply for benefits
- Ask for a contact name and number for a member of staff in the Haematology or Oncology department – Write it in this guide

Patients

- Bring any side effects to the attention of the doctor
- Describe symptoms simply and accurately – do not underplay or exaggerate them
- Take all medication as directed – Use dosette boxes to help remember what to take and when, or ask the pharmacist to write up a chart outlining when to take each medication
- Try to drink three litres of water / liquid each day (unless on a fluid restriction)
- Make getting enough sleep a priority
- Think positively but allow for “off days”
- Keep a diary of symptoms to help learn the pattern and remember to communicate them to the health care team

Carers

- Take care of their own health
- Take some time each day for themselves, preferably out of house if possible
Further information and useful organisations

Myeloma Australia
www.myeloma.org.au
Myeloma Support Nurses 1800 MYELOMA (1800 693 566)

The Cancer Council of Australia
www.cancercouncil.com.au
Cancer Helpline 13 11 20

The Leukaemia Foundation of Australia
www.leukaemia.org.au
Toll free 1800 620 420

International Myeloma Foundation
www.myeloma.org

Myeloma UK
www.myeloma.org.uk

Australian Department of Human Services
www.humanservices.gov.au

Australian Cancer Trials
www.australiancancertrials.gov.au

Australian New Zealand Clinical Trials Registry
www.anzctr.org.au

Carers Australia
www.carersaustralia.com.au

Carers Couch
www.carerscouch.com

EviQ Cancer Treatments online
www.eviq.org.au

Kidney Health Australia
www.kidney.org.au

Lab Tests online
www.labtestsonline.org.au
MSK Cancer Centre About Herbs database
www.mskcc.org

Myeloma and Related Diseases Registry
www.mrdr.net.au

My Aged Care
www.myagedcare.gov.au

National Centre for Complementary and Alternative Medicine
www.nccam.nih.gov

NPS Medicine Wise
www.nps.org.au

Palliative Care Australia
www.palliativecare.org.au
Medical Terms Explained

**Albumin:** Major protein found in the blood. A patient’s albumin level can provide some indication of overall health and nutritional status.

**Alkylating Agent:** A chemotherapeutic agent such as melphalan or cyclophosphamide. Alkylating refers to the way in which these agents cross link the DNA of myeloma cells and block cell division.

**Allogeneic stem cell transplantation:** A procedure in which stem cells or bone marrow from a compatible donor (usually a family member) are collected and given to the patient after high dose chemotherapy treatment.

**AL Amyloidosis:** A condition in which myeloma light chains (Bence Jones proteins) are deposited in tissues and organs throughout the body. This occurs more commonly with lambda versus kappa Bence Jones proteins. In patients with amyloidosis, the light chain proteins bind to certain tissues such as heart, nerves and kidney rather than being excreted out of the body through the kidneys.

**Anaemia:** A decrease in the normal number of red blood cells, or the haemoglobin that they contain, usually below 10g/dl with over 13-14g/dl being normal. Myeloma in the bone marrow blocks red cell production, leading to shortness of breath, weakness, and tiredness.

**Angiogenesis:** Blood vessel formation, which usually accompanies the growth of malignant tissue, including myeloma.

**Antibiotics:** Drugs used to treat infection.

**Antibody:** A protein 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. Others make the antigen more vulnerable to destruction by other white blood cells. In myeloma there is overproduction of non functional antibodies.

**Antigen:** Antigens are molecules on the surface of cells that the immune system recognises.
**Apheresis:** A procedure in which stem cells are collected from the blood using a machine which separates them out, returning the remaining blood components to the donor.

**Apoptosis:** A normal cellular process involving a coordinated series of events leading to the controlled death of a cell.

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

**Asymptomatic myeloma:** See smouldering myeloma

**Autologous stem cell transplant:** A procedure in which a patient’s own stem cells are collected, stored and then given back following high dose chemotherapy.

**Bence Jones:** 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 (<0.1g/24h) can be present in the urine, but this is albumin rather than Bence Jones protein. The presence of any Bence Jones protein is abnormal. See also light chain.

**Beta 2 Microglobulin (β2M):** A small protein found in the blood. High levels occur in patients with active myeloma. Low or normal levels occur in patients with early myeloma and / or inactive disease. Approximately 10% of patients have myeloma that does not produce β2M. For these patients, β2M testing cannot be used to monitor the disease. At the time of relapse, β2M can increase before there is any change in the myeloma protein level. Therefore, 90% of the time, β2M is very useful for determining disease activity.

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

**Bisphosphonate:** A type of drug that binds to the surface of bone where it is being resorbed (or destroyed) to protect it. They include zoledronic acid (Zometa®), pamidronate (Aredia®) and clodronate (Bonefos®). In myeloma, they are used to treat bone disease and protect against further damage.

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

**Blood count:** The number of red blood cells, white blood cells, and platelets in a sample of blood.
**Bone marrow:** The soft, spongy tissue in the centre of bones that produces white blood cells, red blood cells, and platelets.

**Bone marrow aspiration and trephine (BMAT):** The removal, by a needle, of a sample of fluid and bone from the bone marrow for examination under a microscope.

**Calcium:** A mineral important in bone formation. High levels of calcium in the blood can occur when there is bone destruction.

**Catheter:** A tube that is placed in a blood vessel to provide a pathway for treatment with drugs or nutrients. Used during prolonged repeated treatment, a Central Venous Catheter is special tubing that is surgically inserted into a large vein near the heart and exits from the chest or abdomen. The catheter allows medications, fluids, or blood products to be given and blood samples to be taken.

**Cell proliferation:** An increase in the number of cells as a result of cell growth and cell division.

**Chemotherapy:** The treatment of cancer with drugs that kill rapidly dividing cells.

**Chromosome:** A strand of DNA and proteins in the nucleus of a cell. Chromosomes carry genes and transmit genetic information when cells divide. Normally, human cells contain 46 chromosomes.

**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.

**Compassionate access scheme:** A program whereby pharmaceutical companies provide access to new drugs to people fitting certain criteria before they are approved in Australia and available on the Pharmaceutical Benefits Scheme.

**CRAB:** The acronym given to the criteria to help guide doctors in their decisions to start treatment. Calcium elevation; Renal insufficiency; Anaemia; Bone disease.
**C-reactive protein (CRP):** A protein produced by the liver when there is an inflammatory process occurring in the body. The level of CRP in the blood can be raised in various inflammatory diseases, such as infections, and cancers, including myeloma.

**Creatinine:** A small chemical compound normally excreted by the kidneys. If the kidneys are damaged, the level of creatinine builds up, resulting in an increased serum creatinine. The serum creatinine test is used to measure kidney function.

**CT or CAT (Computerised Tomography) scan:** A test using Computerised 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. Also called CAT (Computed Axial Tomography) scan.

**Cytokine:** A substance secreted by cells of the immune system that stimulates growth / activity in a particular type of cell.

**Cytogenetics:** A laboratory test on plasma cells to determine if there are any abnormalities in the chromosomes.

**DEXA Scan (Dual Photon X-ray Absorptiometry) study:** The best measure of bone density. Used to reveal amount of bone loss.

**Dexamethasone:** A powerful steroid given alone or with other drugs.

**Dialysis:** When a patient’s kidneys are unable to filter blood, the blood is cleaned by passing it through a dialysis machine.

**DNA:** Or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms.

**Electrophoresis:** A laboratory test in which a patient’s serum (liquid portion of blood) or urine molecules are subjected to separation according to their size and electrical charge. For myeloma patients, 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 protein type (M-spike) characteristic for each patient. Electrophoresis is used as a tool both for diagnosis and for monitoring.
**Engraftment**: The process by which transplanted stem cells travel to the recipient’s bone marrow where they will begin to grow and develop into new blood cells. During this time the number of red cells, white cells and platelets in the blood may be lower than normal.

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

**Erythrocytes**: Red blood cells (RBCs). RBCs carry oxygen in the form of haemoglobin to body cells and carry carbon dioxide away from body cells.

**Erythropoietin (EPO)**: A hormone produced by the kidneys. Myeloma patients with damaged kidneys don’t produce enough erythropoietin and can become anaemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency. Synthetic erythropoietin is being used prophylactically before chemotherapy and as a supportive therapy after chemotherapy to avoid anaemia.

**FISH**: Fluorescent In-situ hybridisation.

**Free Light Chains**: See serum free light chains.

**Graft versus host disease (GvHD)**: A complication of allogeneic transplants whereby the donor cells (the graft) recognises the recipient’s body (the host) as foreign and mounts an attack. This can cause skin, liver and gut problems, and is usually treated with steroids that suppress the immune system.

**Growth factor (G-CSF)**: Granulocyte Colony Stimulating Factor is a protein used to promote white cell production in the bone marrow. It is given as an injection into the skin (sub cutaneous).

**Heavy Chain**: See immunoglobulin.

**Hypercalcaemia**: A higher than normal level of calcium in the blood. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. Common in myeloma patients and usually resulting from bone destruction with resultant release of calcium into the blood stream. Often associated with reduced kidney function since calcium can be toxic to the kidneys. For this reason, hypercalcaemia is usually treated on an emergency basis using intravenous fluids combined with drugs to reduce bone destruction and direct treatment for the myeloma.
**Immunoglobulin (Ig):** A protein that is produced by plasma cells for a variety of purposes, most commonly to fight infection. There are five main types; IgA, IgD, IgE, IgG and IgM. See also antibody.

**Immunosuppression:** Lowering the number or activity of cells that make up the immune system, primarily the white cells. Suppression of the immune system can mean an increased risk of infection.

**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.

**Interferon:** A naturally produced hormone (cytokine) released by the body in response to infection or disease, which stimulates the growth of certain disease fighting blood cells in the immune system. Interferon can be artificially synthesised and used as a form of immunotherapy, primarily in the maintenance (plateau) phase to block any regrowth of myeloma and thus delay or prevent relapse.

**Kappa:** See light chain.

**Lambda:** See light chain.

**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. See lytic lesion.

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

**Leukopenia:** A low number of white blood cells.

**Light chain:** One of the short protein chains that make up an immunoglobulin molecule. May be referred to as kappa or lambda type. Light chains produced by myeloma cells are also referred to as Bence Jones proteins after the man who first identified them.

**Lymphocytes:** A type of white blood cell that fights infection and disease.

**Lytic 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.

**M proteins (M spike):** Antibodies or parts of antibodies found in unusually large amounts in the blood or urine of myeloma patients. M spike refers to the sharp pattern that occurs on protein electrophoresis when an M protein is present. Synonymous with monoclonal protein, paraprotein and myeloma protein.

**MRI (Magnetic resonance imaging):** An imaging technique that provides detailed images of bone and soft tissue.

**MGUS:** Monoclonal Gammopathy of Undetermined Significance is a premalignant disorder characterised by the accumulation of plasma cells within the bone marrow and the presence of a monoclonal protein spike on electrophoresis. The feature that distinguishes it from myeloma is the lack of end organ damage. What this means is that there are no lytic bone lesions, no renal damage and no anaemia. The condition is stable and requires no treatment, only monitoring. By 10 years of follow-up approximately 10-20% of patients progress to clinical myeloma.

**Mini-allogeneic transplant:** A type of allogeneic transplant that uses lower doses of chemotherapy than a standard allogeneic transplant, and avoids some of the side effects and risks associated with higher dose chemotherapy.

**Mobilisation:** The process by which the number of stem cells in the bone marrow is increased so that they ‘spill over’ into the blood stream and can be collected.

**Monoclonal:** A clone or duplicate of a single cell. Myeloma develops from a single malignant plasma cell (monoclonal). 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 is that it shows up as a sharp spike (M spike) in the serum electrophoresis test.

**Mucositis:** Inflammation of the lining of the digestive tract, often seen as soreness of the mouth. Can occur as a side effect of chemotherapy.

**Myeloma Related Event (MRE):** Criteria used by doctors to help decide when treatment should begin. Often used interchangeably with the acronym CRAB.

**Neoplasm:** A new growth of tissue or cells; a tumour that can be referred to as benign or malignant.
Neutrophils: A type of white blood cell (leucocyte) necessary to combat bacterial infection.

Neutropenia: A low number of neutrophils in the blood, which can lead to an increased risk of infection. Can be caused by the myeloma itself or as a side effect of treatment, particularly chemotherapy. Sometimes treated with a growth factor that can boost the number of neutrophils (G-CSF). See growth factor.

Osteoblast: Bone forming cells.

Osteoclast: Cells that resorb or break down bone. Found in the bone marrow at the junction between the bone marrow and the 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 condition in which regions of the bones of the jaw fracture and do not heal properly, causing ongoing, sometimes painful, complications.

Palliative treatment/care: Aimed at improving the quality of life by relieving pain and symptoms of disease but not altering its course.

Paraprotein: See M protein.

Pathological fracture: A break in a bone usually caused by cancer or some disease condition. Occurs in myeloma-weakened bones which can’t bear normal weight or stress.

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

Peripherally Inserted Central Catheter (PICC): A small tube (catheter) inserted into a small blood vessel in the arm that extends into a larger blood vessel in the chest. Used as a longer term device to enable the administration of intravenous drugs and blood products. Can remain in place for many months and reduces the need for repeated cannulation (insertion of small, disposable needle, lasting < 72 hours). See also catheter.

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 (i.e. anaemia, kidney damage, and nerve damage).

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

**Plasmapheresis**: The process of removing certain proteins from the blood. Plasmapheresis can be used to remove excess antibodies from the blood of multiple myeloma patients.

**Platelet**: Small cell fragments in the blood that helps it to clot. Also called thrombocytes.

**Radiation therapy (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).

**Red blood cells (RBC)**: See erythrocytes.

**Reduced intensity conditioning (RIC)**: Lower doses of chemotherapy or radiation prior to an allogeneic transplant. This regime is less toxic and more easily tolerated than full intensity conditioning.

**Related Organ Tissue Injury (ROTI)**: An acronym describing specific impairments to the optimal functioning of the body that help doctors decide when treatment should begin. The term is used interchangeably with MRE and CRAB.

**Serum**: Liquid portion of blood remaining after blood has been allowed to clot and the clot removed.

**Serum Free Light Chains (SFLC)**: A portion of the monoclonal protein of light molecular weight that can be measured in a sensitive assay, the Freelite™ test.

**Sestamibi scan**: Is a scanning technique using an injection of a radiolabeled isotope to help detect myeloma deposits that may not be detected by other imaging techniques.
**Skeletal survey (bone survey):** A series of X-rays of the skull, spine, ribs, pelvis and long bones to look for lytic lesions and/or osteoporosis.

**Smouldering myeloma:** In this condition there is evidence of plasma cells in the bone marrow and a measurable paraprotein with minimal end organ damage. These levels are not stable and will eventually progress to myeloma. Conventionally, treatment is withheld until there is significant evidence of disease progression.

**Stem cells:** The immature cells from which all blood cells develop. Normal stem cells give rise to normal blood components, including red cells, white cells, and platelets. Stem cells are normally located in the bone marrow and can be harvested for transplant.

**Thrombocytopenia:** A low number of platelets in the blood. The normal level is 150,000 - 250,000. If the platelet count is less than 50,000, bleeding problems could occur. Major bleeding occurs when the platelet count is 10,000 or less.

**Vertebroplasty:** The injection of surgical cement into the vertebral space to reduce the pain caused by vertebral compression fracture.

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

**White blood cells:** See leucocytes.
Appendices

Appendix 1: Table of commonly used medications

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Trade Name</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>Velcade®</td>
<td>Anti myeloma drug belonging to a group of drugs called proteasome inhibitors</td>
</tr>
<tr>
<td></td>
<td>IV/SC</td>
<td></td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>Kyprolis®</td>
<td>Anti myeloma drug belonging to group of drugs called proteasome inhibitors</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Clodronate</td>
<td>Bonefos®</td>
<td>Bisphosphonate drug. Protects bones from further damage by myeloma cells.</td>
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<tr>
<td></td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Cycloblatin®</td>
<td>Anti myeloma chemotherapy drug. Often in combination with other anti myeloma drugs</td>
</tr>
<tr>
<td></td>
<td>IV / O</td>
<td></td>
</tr>
<tr>
<td>Doxorubacin</td>
<td>Adriamycin®</td>
<td>Anti myeloma drug. Often in combination with other anti myeloma drugs</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Daratumumab</td>
<td>IV</td>
<td>Monoclonal antibody</td>
</tr>
<tr>
<td>Etoposide</td>
<td>IV</td>
<td>Anti myeloma drug. Often in combination with other anti myeloma drugs</td>
</tr>
<tr>
<td>Elotuzumab</td>
<td>IV</td>
<td>Monoclonal antibody</td>
</tr>
<tr>
<td>Granulocyte colony stimulating factor (G-CSF)</td>
<td>Filgrastim®</td>
<td>A protein that stimulates the development and growth of white blood cells. Used to stimulate the growth of stem cells before harvesting for transplantation or to boost white cells if they are reduced in number</td>
</tr>
<tr>
<td></td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td>Neupogen</td>
<td>Neulasta®</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td><strong>Idarubicin</strong></td>
<td>Zavedos* IV / O</td>
<td>Anti myeloma chemotherapy drug given in combination with other anti myeloma drugs.</td>
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<tr>
<td>---------------</td>
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<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Ixazomib</strong></td>
<td>Ninlaro O</td>
<td>Anti myeloma drug in the group of drugs called proteasome inhibitors. Often given in combination with other anti myeloma drugs.</td>
</tr>
<tr>
<td><strong>Lenalidomide</strong></td>
<td>Revlimid* O</td>
<td>Anti myeloma drug chemically similar to thalidomide, lenalidomide is a 2nd generation immunomodulatory drug (IMiD) that works by affecting and modifying the immune system. The exact way in which IMiDs work is not yet fully understood and it is thought they have multiple mechanisms of action.</td>
</tr>
<tr>
<td><strong>Melphalan</strong></td>
<td>Alkeran* IV / O</td>
<td>Anti myeloma drug. Given in combination with other anti myeloma drugs or in high dose intravenously as part of the stem cell transplant process.</td>
</tr>
<tr>
<td><strong>Metoclopramide</strong></td>
<td>Maxolon* / Pramin*</td>
<td>Anti nausea medication. Often given as tablets to help prevent nausea associated with medications</td>
</tr>
<tr>
<td><strong>Oxycodone hydrochloride</strong></td>
<td>Endone*</td>
<td>Pain medication.</td>
</tr>
<tr>
<td><strong>Pamidronate</strong></td>
<td>Aredia*</td>
<td>Bisphosphonate drug. Given intravenously to protect bones from further damage by myeloma cells.</td>
</tr>
<tr>
<td><strong>Pomalidomide</strong></td>
<td>Pomalidomide</td>
<td>3rd generation immunomodulatory drug (IMiD) that works by affecting and modifying the immune system. The exact way in which IMiDs work is not yet fully understood and it is thought they have multiple mechanisms of action.</td>
</tr>
</tbody>
</table>
Thalidomide | Thalomid® 1st generation immunomodulatory drug (IMiD) that works by affecting and modifying the immune system. The exact way in which IMiDs work is not yet fully understood and it is thought they have multiple mechanisms of action.

Appendix 2: Tests and investigations

| Bone marrow biopsy | This is the single most critical test to determine the percentage of myeloma cells in the bone marrow. For solitary plasmacytoma, direct biopsy of the tumour mass is often performed. Chromosome analysis (cytogenetic testing) can reveal good or poor chromosome features using direct and / or fluorescent in situ hybridization (FISH) analysis. |
| Special testing is done to assess prognosis (e.g. chromosomes, immune typing, staining for amyloid) |

Blood Testing

1. Full blood count
   - To assess presence / severity of anaemia
   - To assess for low white cell count
   - To assess for low blood platelet count

2. Chemistry panel
   - Particularly important to assess kidney function (creatinine), calcium level and lactate dehydrogenase (LDH)

3. Special protein testing
   - Serum protein electrophoresis (SPEP), Serum Free Light Chain (SFLC), immunoelectrophoresis (IFE).Freelite
   - This shows the presence of the abnormal paraprotein
     - The amount of abnormal M protein as well as the normal albumin protein level are measured
     - Shows the type of M protein
     - SFLC testing can be used to measure the amount of free Kappa or Lambda protein
<table>
<thead>
<tr>
<th>Urine Testing</th>
<th>Shows the presence, amount, and type of abnormal myeloma protein in the urine (Bence Jones)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special protein testing as for the blood:</td>
<td></td>
</tr>
<tr>
<td>Urine Protein Electrophoresis</td>
<td></td>
</tr>
<tr>
<td>Immunofixation</td>
<td></td>
</tr>
<tr>
<td><strong>Bone imaging</strong></td>
<td>To assess the presence, severity, and location of any areas of bone damage.</td>
</tr>
<tr>
<td><strong>X-Rays</strong></td>
<td>Whole body Xrays (skeletal surveys) are no longer the gold standard in searching for myeloma bone damage in the skeleton. The more sensitive test, a whole body low dose CT is now recommended. Xrays may still be useful at imaging bones from time to time.</td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td>Used for more detailed testing of particular areas such as spine and/or brain. Can reveal the presence and distribution of disease in the bone marrow. Can also reveal disease outside of bone, which may be pressing on nerves and/or spinal cord</td>
</tr>
<tr>
<td><strong>CT Scan</strong></td>
<td>Whole body low dose CT is recommended for assessing the skeleton for myeloma bone damage. Especially useful for detailed evaluation of small areas of possible bone damage or nerve pressure</td>
</tr>
<tr>
<td><strong>Whole Body FDG / PET (fluorodeoxyglucose positron emission tomography) scan</strong></td>
<td>A much more sensitive whole body scanning technique that shows areas of active myeloma, it is useful for disease monitoring, especially for non-secretory disease.</td>
</tr>
<tr>
<td><strong>Sestamibi scan</strong></td>
<td>A scanning technique that uses a small amount of radioactive material (radiotracer) to help find myeloma deposits that are not found using other scanning techniques. Not a common test for myeloma.</td>
</tr>
</tbody>
</table>
## Appendix 3: Blood tests

<table>
<thead>
<tr>
<th>Blood tests</th>
<th>Test Name</th>
<th>Normal range*</th>
<th>Units</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full Blood Count</strong></td>
<td>White cell count</td>
<td>4.0 – 10.0</td>
<td>X10⁹/l</td>
<td>A low count makes the body less able to fight infection</td>
</tr>
<tr>
<td>Haemoglobin (men)</td>
<td></td>
<td>130-170</td>
<td>g/l</td>
<td>A low haemoglobin is also anaemia, causing fatigue</td>
</tr>
<tr>
<td>Haemoglobin (women)</td>
<td></td>
<td>115-150</td>
<td>g/l</td>
<td>A low haemoglobin is also anaemia, causing fatigue</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>150-400</td>
<td>X10⁹/l</td>
<td>A low count makes the body bruise or bleed easily</td>
</tr>
<tr>
<td><strong>Urea, creatinine and electrolytes</strong></td>
<td>Urea</td>
<td>3-8</td>
<td>mmol/l</td>
<td>Measure of kidney function</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>50-90</td>
<td>umol/l</td>
<td>Measure of kidney function</td>
</tr>
<tr>
<td>Calcium (total)</td>
<td></td>
<td>2.15-2.55</td>
<td>mmol/l</td>
<td>Raised by myeloma bone disease</td>
</tr>
<tr>
<td><strong>Proteins</strong></td>
<td>Albumin</td>
<td>40-50</td>
<td>g/l</td>
<td>Often lowered in myeloma because of presence of paraprotein</td>
</tr>
<tr>
<td>Total protein</td>
<td></td>
<td>60-80</td>
<td>g/l</td>
<td>Often raised in myeloma because of amount of paraprotein</td>
</tr>
<tr>
<td>Paraprotein</td>
<td></td>
<td>0</td>
<td>g/l</td>
<td>Abnormal protein found in several conditions, including myeloma.</td>
</tr>
</tbody>
</table>

The normal range is an average: each hospital laboratory has its own ‘normal range’ of values.
**Explanation of units**

- g/dl  how many grams there are in a decilitre (one tenth of a litre) of blood
- g/l  how many grams there are in a litre of blood
- x10^9/l  how many thousand million cells there are in a litre of blood
- x10^12/l  how many million million cells there are in a litre of blood
- mmol/l  how many thousandths of a mole** in a litre of blood
- umol/l  how many millionths of a mole** there are in a litre of blood

**mole a standard molecular measurement for the amount of any chemical**

Note: Doctors do not use a litre of blood to make these measurements; they just take a small sample (a few millilitres) and then multiply the results.
Contact Details

Fill in your contact details and those of the key health professionals involved in your care. You may like to include numbers for working hours and out of hours hospital contacts.

Name: _____________________________________________________________________________________

Address: ___________________________________________________________________________________

____________________________________________________________________________________________

Tel no: _____________________________________________________________________________________

Email: _____________________________________________________________________________________

Hospital medical registration number (if known): __________________________________________

Healthcare team

Haematologist / Oncologist: _______________________________________________________________

Tel no: ___________________________________________________________________________________

Treatment centre: _________________________________________________________________________

During working hours Tel no: ______________________________________________________________

Out-of-hours Tel no: _______________________________________________________________________

Nurse Specialist / Coordinator: ____________________________________________________________

Tel No: __________________________________________________________________________________

Pharmacist: _______________________________________________________________________________

Tel no: ___________________________________________________________________________________

GP: _____________________________________________________________________________________

Tel no: __________________________________________________________________________________
To discuss any of the information contained in this guide, or further assistance, please call the Myeloma Support Line on 1800 MYELOMA (1800 693 566)

A Myeloma Support Nurse will answer your call in confidence.