RELAPSED AND REFRACTORY MYELOMA

Myeloma Australia

Your questions answered

Myeloma Australia

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 families, 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.

If you would like to talk to someone about any aspect of myeloma, its treatment and management, you can call our free Telephone Support Line on

1800 MYELOMA (1800 693 566)

A Myeloma Support Nurse will answer your call in confidence and address your questions. They can also connect you with support services in your area. The service is available during business hours Monday to Friday (AEST). You can also access more information and support services by visiting www.myeloma.org.au

This booklet provides general information about relapsed and refractory myeloma and is not intended to replace medical care or the advice of your treating team.

Please talk to your doctor if you have any questions about your diagnosis or treatment. Your doctor can answer your questions, talk with you about your treatment goals, and provide you with extra support.

Important note

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, reviewers, nor the publishers accept any legal responsibility for the content. It is strongly recommended that individuals seek advice directly from medical professionals for information that applies to their individual circumstances.

Thank you

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Thank you to Myeloma UK whose *Infopack for relapsed and/or refractory myeloma patients* provided the initial inspiration for this booklet.

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Myeloma Australia acknowledges that our office is located on the lands of the Bunurong Boon Wurrung and Wurundjeri Woi Wurrung peoples of the Eastern Kulin Nation and pays respect to their Elders past, present and emerging.

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About this booklet

Learning that your myeloma has relapsed or has become refractory to treatment is an understandably challenging and emotional time.

You may be experiencing a whole range of thoughts and feelings – disappointment, anger and sadness – but perhaps feeling hopeful about starting active treatment to give you more control over the disease.

You may also have questions about why your myeloma has come back or has stopped responding to treatment – and wondering what the next stage of treatment will hold for you.

It is helpful to know that it is very normal to feel this way and to ask these questions.

We have written this booklet for people living with myeloma, as well as their families, carers and friends, to help answer many of your questions and to find the support you need at this time.

When you understand more about myeloma and the pattern that it follows, how it may affect you and the considerations for your treatment, it can help you to feel confident that you and your treating team are taking positive steps together.

Thankfully, there are many different treatment options available through the Pharmaceutical Benefits Scheme, clinical trials, or other access schemes. You will find information about many of these treatments in the 'Resources' section of www.myeloma.org.au

There is much more to learn about myeloma and so we have suggested other resources you can read throughout this booklet. You can find these on our website or by contacting our friendly staff.

Our aim is to help support you at each step of your treatment pathway, helping you to work with your treating team and live as well as you can. Please remember to ask for the support you need, and know that you can talk to our Myeloma Support Nurses on our Telephone Support Line or at information and support group.

> *At my first relapse, my haematologist reassured me he had many tools in the toolbox. With this, I remain hopeful and just take one day at a time and enjoy my life as best I can.*
>
> **- William, New South Wales**

What's covered in this booklet

Things to remember

- Relapsed myeloma is when the disease becomes active again and needs treatment.
- Refractory myeloma is when the disease does not respond to the chosen treatment at all, or the treatment works for some time and then stops working.
- While myeloma cannot be cured, there are many new clinical trials and treatments that are able to slow its progress, put you back into remission or plateau phase, control symptoms, and give you the best quality of life for as long as possible.
- Learning that your myeloma has relapsed or has become refractory to a treatment is an understandably challenging and emotional time. Ask for support when you need it and remember that these feelings will usually ease with time as you begin to adapt to this new stage of living with myeloma.
- Your doctor will talk with you about the different treatment options available, and their benefits and risks.
- Having your blood tests at the recommended time points will help you and your doctor to monitor and manage your myeloma.
- Always let your healthcare professional know if you develop any new symptoms or side effects, if you have any concerns, or need extra support.

A quick recap on myeloma

Myeloma, also known as multiple myeloma, is a type of blood cancer that starts in plasma cells, which are normally found in the bone marrow. Plasma cells form part of our immune system. Normal plasma cells produce different types of antibodies (also called immunoglobulins) to help fight various infections.

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. Myeloma is often diagnosed and monitored by measuring this paraprotein in the blood.

There are many different types and subtypes of myeloma, and these are named after the type of paraprotein that the myeloma cells are producing – made up of different heavy and light chains. Sometimes, there is no paraprotein produced, but the light chains detach from the heavy chains and can be measured in the blood. This is called light chain myeloma. Our *Understanding Paraprotein in Myeloma* information sheet explains more about this complex but important concept. While the progress of myeloma and its response to treatment can be monitored by following both paraprotein and free light chain levels, we have kept things simple in this booklet, and have talked about paraprotein only as a way of referring to myeloma's response to treatment.

Bone marrow biopsies at diagnosis and at regular intervals measure your total number of plasma cells. Scans are used to look for areas of bone that may be affected by the myeloma. The most common areas are where bone marrow is usually active – such as bones in the spine, pelvis, ribcage, shoulders and hips.

Myeloma can also affect bone marrow function, resulting in anaemia, and affect kidney function, it can also cause high levels of calcium in the blood.

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, which can result in a disease plateau or remission, it is important to have regular monitoring to watch for when the myeloma returns, which is called a relapse or progressive disease. When myeloma is under control, people usually return to a good state of health which can last from months to years.

With many new developments in its treatment and management, the outlook for myeloma is improving all the time. Research is continuing to develop new treatments and find ways to use existing treatments effectively.

These advances are having a very positive impact on survival rates, and people with myeloma are now living longer than ever before.

Understanding relapsed and refractory myeloma

What is relapsed myeloma?

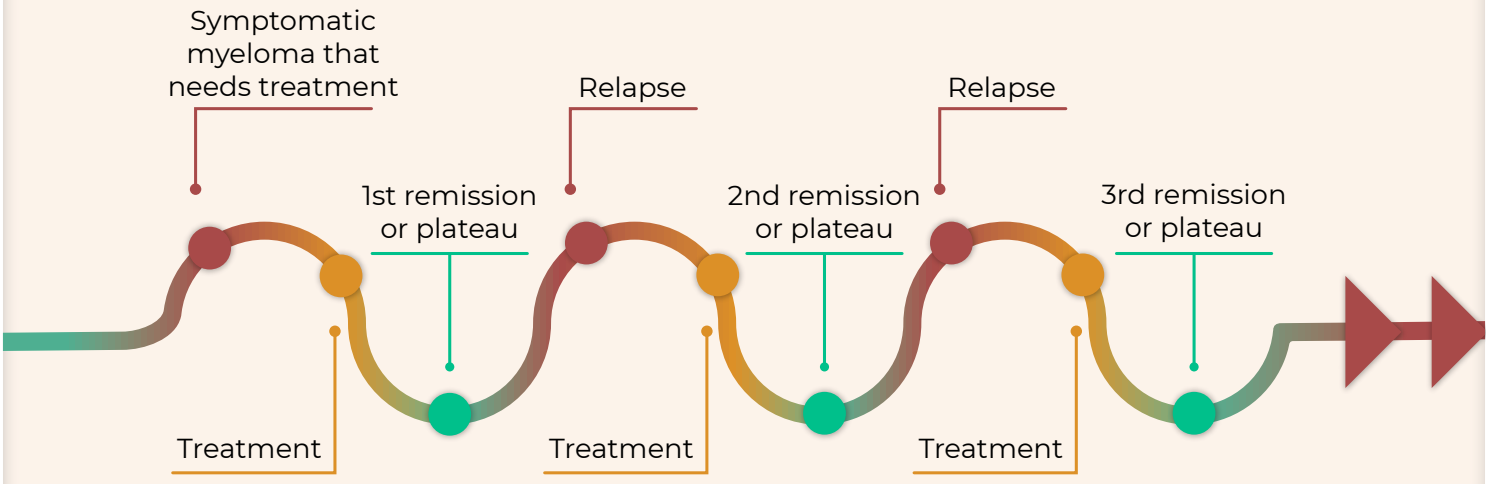
Myeloma is a relapsing-remitting cancer – a cancer that continues to come back and then go back under control again – which makes it different from many other cancers.

There will be periods when your myeloma is active: this means that it is detectable in your blood and bone marrow, or you have symptoms such as bone pain, anaemia or lethargy.

This is when treatment is necessary to bring your myeloma under control.

In some cases, the treatment will reduce the amount of myeloma until it is no longer detectable, and your symptoms have gone away. This is called a period of remission.

The relapse and remission cycle



Note that the number of relapses and the time between relapses will be different for each person with myeloma.

You can read more about myeloma and its treatments in our book, Myeloma – A Comprehensive Guide.

Different types of responses to initial myeloma treatment

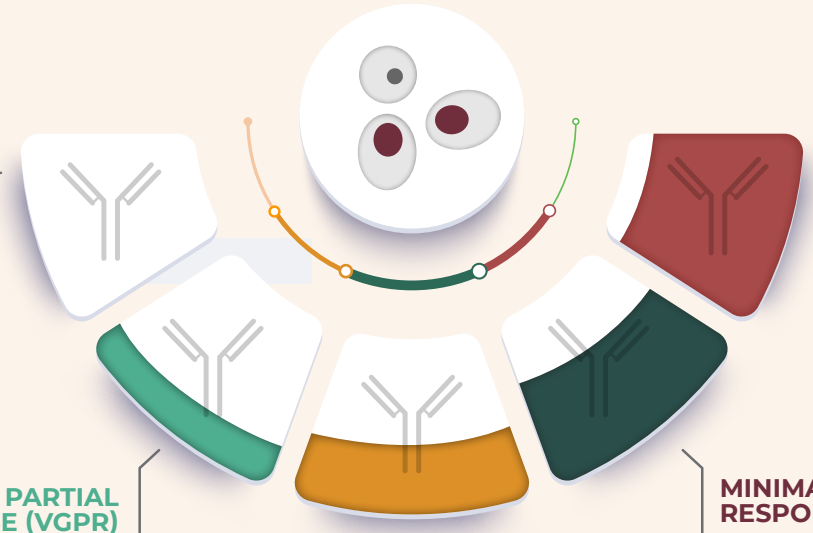
When there is no myeloma detectable, your doctor may tell you that you have had a complete response. However, it's important to know that not everyone achieves a complete response from their treatment. Depending on the number of plasma cells in your bone marrow, the level of paraprotein in your blood and the presence of bone disease, a person may have a very good partial response, partial response, minimal response or stable disease. We have described these different responses in the diagram below.

Many people can live with a certain level of myeloma in their blood and bone marrow, often for a long time, without it causing any problems. This is called a plateau period.

No matter what type of initial response you have had to treatment, your doctor will continue to monitor your myeloma to look for signs that myeloma is active again or that you have "progressive disease".

When myeloma has relapsed, it means it has become active again and higher levels of paraprotein can be detected in your blood, more plasma cells can be found in your bone marrow, or you are experiencing symptoms like bone pain

Different responses to treatment



COMPLETE RESPONSE (CR)
No paraprotein detectable And/or negative immunofixation test

STABLE DISEASE (SD)
Less than 25% paraprotein decrease, but disease is not progressive

VERY GOOD PARTIAL RESPONSE (VGPR)
No paraprotein detectable. But positive immunofixation test OR 90% paraprotein decrease

MINIMAL RESPONSE (MR)
25 - 49% paraprotein decrease

PARTIAL RESPONSE (PR)
≥ 50% paraprotein decrease

Margaret's experience with relapsed myeloma

After completing her initial treatment with bortezomib, Margaret had not been on any treatment for myeloma and her paraprotein was undetectable in monthly blood tests.

Recently, Margaret's paraprotein started to rise again. This meant that her myeloma had relapsed, and so her doctor recommended starting the next treatment.

What is refractory myeloma?

Refractory myeloma is another way of saying the myeloma is resistant to a chosen treatment.

In some people, myeloma does not respond to the chosen treatment at all. In other people, the treatment may work for some time and then stop working (relapsed and refractory), or their myeloma may progress soon after their last dose of treatment.

These are all types of refractory myeloma, or myeloma that has become refractory to treatment.

If your myeloma is refractory to treatment, your doctor will change your treatment. Most of the time, myeloma will respond to the next treatment.

A lot of the information about relapsed myeloma in this booklet is also relevant to refractory myeloma.

Chen's experience with refractory myeloma

Chen was diagnosed with myeloma and started his first line of treatment. After the first two cycles of treatment, his paraprotein remained the same. After the third cycle of treatment, his paraprotein began to increase: his myeloma was not responding to this treatment combination – it had become refractory to the treatment.

Chen's haematologist changed him to a different type of treatment and, much to Chen's relief, his paraprotein started to reduce.

Ian's experience with relapsed and refractory myeloma

Ian was diagnosed with myeloma and had a very positive response to his first line of treatment.

He was then prescribed maintenance therapy, which kept his myeloma under control for a good length of time.

Ian's paraprotein then started to rise and continued rising until it had doubled. His doctor explained that the myeloma had relapsed and was now refractory to the maintenance therapy – and so it was time to change to a new type of treatment.

Why does relapse happen?

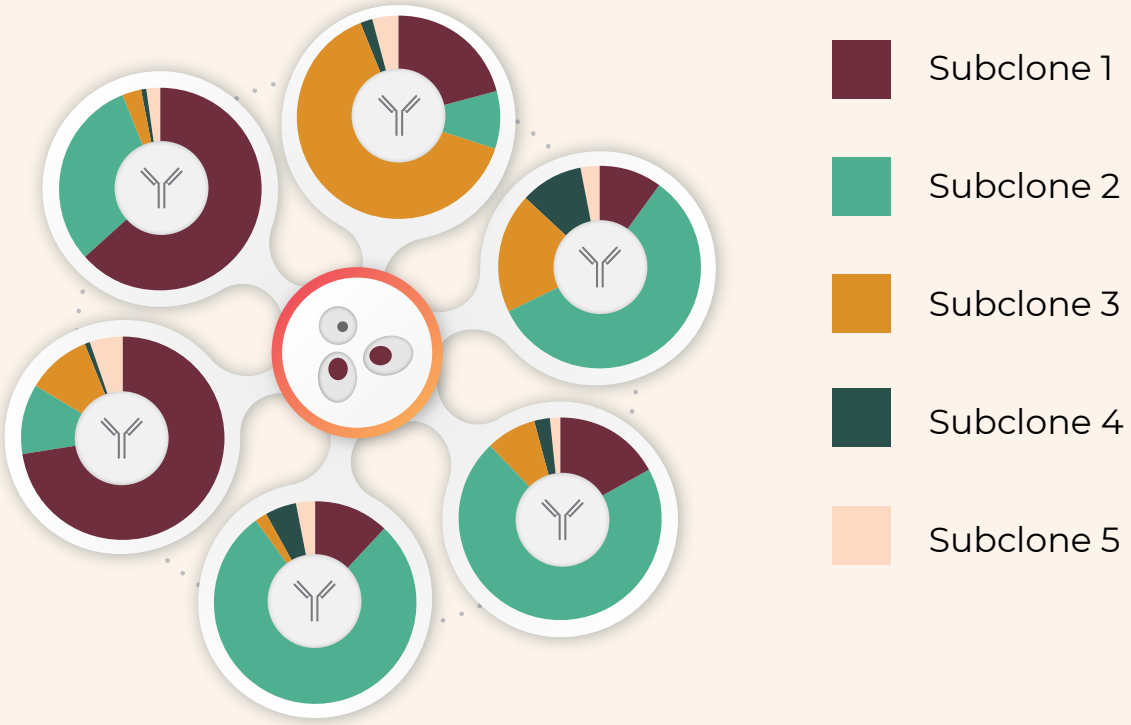
In myeloma, plasma cells have become damaged or cancerous. These cells multiply faster than the healthy plasma cells. The damaged cells can vary in their genetic makeup, producing slightly different versions of themselves, called subclones. During each active phase of myeloma, there will usually be one or more dominant subclones that are detectable in the bone marrow that cause symptoms.

Treatments for myeloma can be very effective at reducing the dominant subclone. However, some of the other subclones may be resistant to treatment. They can lay dormant for a long time, but eventually become active, leading to relapse and the need for your next treatment.

When myeloma returns, it may be the same subclone that was detected at diagnosis – or it may be a different subclone that has become dominant or detectable. This is why it is possible for myeloma to change the way it behaves. For example, in the beginning, the myeloma cells may only produce an abnormal paraprotein. Then at relapse, you may develop higher levels of light chains that were not present when you were diagnosed. Your doctor is always monitoring you to look for these possible changes.

There is currently no way of predicting when myeloma will come back, but it helps to know that periods of response or stable disease can last from months to many years.

Subclones in myeloma



This diagram represents the different subclones, and how the dominant subclone can change with each relapse.

What is minimal residual disease and why is it important?

There can be some low-level disease in the bone marrow, even when you have had a complete response to treatment. This low-level disease is not usually visible through conventional tests and is known as minimal residual disease (MRD).

Doctors increasingly believe that being able to assess MRD may help to predict when you will relapse. This may ultimately help to develop personalised treatment plans in the future.

Specialised tests that are being used to look for evidence of MRD include flow cytometry (which uses proteins expressed on plasma cells to identify small numbers in the bone marrow not visible using microscopy), genetic tests, and improved scanning techniques.

To read more about MRD, see the International Myeloma Foundation's Black Swan Research Initiative at www.myeloma.org

How will I know if I am relapsing?

At relapse, some people may experience symptoms of myeloma, such as new or increased bone pain, overwhelming fatigue, or recurrent infections. These might be the same symptoms you had at diagnosis, or they may be different.

Other people may not have any signs or symptoms, but the paraprotein levels in their blood and/or urine will start to rise. This is called a biochemical relapse.

It is extremely important to maintain a relationship with your doctor and report any new symptoms you have. It is also important to have regular blood tests. Your doctor will decide how often you need to have these tests based on your individual situation.

Your blood tests will look for any signs of myeloma, and also monitor your red blood cells, white blood cells, platelets, electrolytes, and kidney and liver function.

> *I was symptomatic with new bone pain, so my doctor did a PET scan and found new lytic lesions which were not present at my diagnosis.*
>
> - Dee, Tasmania

> *I experienced bone pain and a low blood count when I was diagnosed, but when I relapsed the only sign was in my bloods. I was happy that we were able to treat it early and I felt well and had no symptoms.*
>
> - Alfonso, Queensland

To learn more about the signs and symptoms of myeloma and common tests, see our book, Myeloma – A Comprehensive Guide.

Making treatment choices

Treatment for relapsed myeloma

When myeloma returns, your doctor will organise additional tests such as a bone marrow biopsy and will talk with you about treatments to help regain control of the disease.

Your doctor may have discussed these treatment options as part of your initial treatment plan. However, because available treatment options and your personal circumstances may have changed, it may be necessary to discuss all the options again. In some people, the original treatment can be repeated successfully, especially if you had a good initial response to it.

Treatment is not always necessary at the first sign of relapse. Sometimes, myeloma progresses very slowly. Even if there are signs of myeloma returning in your blood, bone marrow or urine, you may not need to start treatment straight away.

Your doctor will monitor how quickly the paraprotein is rising and only recommended starting treatment once it has reached a certain level or pace of progression.

Please talk with your doctor about the level or pace that that applies for you.

> *Compared to my initial diagnosis, there were more considerations that my doctor and I workshopped together to make a decision around my next treatment phase.*
>
> - Lilian, NSW.

Considerations before starting a new treatment

When starting treatment for a relapse, you and your doctor will need to consider:

- if this is your first or later relapse
- which treatments you previously had and how well you responded to these
- if you are resistant or refractory to any treatment
- the length of your response after your previous treatment
- if you have any long-term side effects from treatment, such as peripheral neuropathy (nerve pain)
- if you are experiencing any myeloma-related complications, such as kidney problems
- your general health
- your age
- your priorities and preferences
- availability of treatments on the Pharmaceutical Benefits Scheme (PBS)
- availability of clinical trials and your interest in taking part
- whether you may be eligible for another stem cell transplant – if you had a successful autologous stem cell transplant in your initial treatment, you may have enough stem cells stored that can be used for another transplant, if you still fit the eligibility criteria and it is an option you'd like to consider.

Treatment for refractory myeloma

If you have refractory myeloma, where the disease did not respond or stopped responding to a previous treatment, then your doctor will talk to you about using a different treatment.

With refractory disease, your doctor will consider many of the same factors as when treating relapsed disease. Your doctor will also consider how they might be able to overcome your myeloma's treatment resistance by changing doses, adding in another medicine, or changing combinations of medicines.

Clinical trials

Clinical trials are a good way to gain early access to new treatments or new combinations of treatments. These advantages need to be weighed up against the location of the clinical trial and the commitment required for you to be involved.

Each clinical trial has its own set of inclusion and exclusion criteria. Ask your doctor if you are eligible for any clinical trials in your area and then talk about whether it is the right choice for you.

> *Initially my myeloma was stubborn, and I was refractory to the treatment. However, I was given the option of a clinical trial and my myeloma has responded beautifully.*
>
> **-Vicki, Western Australia**

Supportive therapy

Supportive therapy is the term used for treatments used to manage the symptoms and complications of myeloma. This may be to prevent infections, support bone health or manage the ongoing side effects of treatment.

Effectively managing these symptoms and complications is essential for your quality of life and is just as important as treating your myeloma.

Our books, *Myeloma – A Comprehensive Guide* and *Living Well with Myeloma* include more information on supportive therapies and provide helpful tips for daily living.

Remember that there are many effective treatments for relapsed and refractory myeloma: these include existing treatments and new medicines that are being developed and tested.

Questions to ask your treating team

It can be very helpful to write down questions that you would like to ask your health professionals about your new treatment and take this list to your appointments.

Here are some examples of questions you might like to ask:

- What are all my treatment options?
- Is there a clinical trial available that is suitable for me?
- Which of these treatment options do you recommend for me and why?
- Do I need to start treatment straight away?
- What are the possible side effects of these treatments?
- How can I prevent and manage side effects?
- What should I do if I have a side effect or symptom that is new or getting worse?
- What should I do if I have a fever?
- Will this treatment affect my ability to have children?
- How often will I need to come to hospital for my treatment?
- How is the treatment given? How long will it take?
- Are there any out-of-pocket costs to me for this treatment?
- How often will I need to have blood tests?
- Do I need a pathology request form today?
- Do I need to have bone-strengthening medicine while on this treatment?
- Are there any other supportive care medicines I need to take?
- When will I see my doctor again?
- What is the contact number for the hospital where I will have treatment?

Coping with the news

Everyone deals with the news that their disease has relapsed or become refractory to treatment in different ways. People often say that being told their myeloma has returned, or is not responding to treatment, is worse than being told of their initial diagnosis. It is normal to feel many mixed emotions, and these may change over time from disappointment to anger and sadness.

For example, you may feel disappointed that you did not remain in remission for the period of time you had expected. Or you may feel sad that your treatment has changed, impacting on your plans with family or friends. If your myeloma has become refractory to a treatment, you may feel angry that it hasn't worked.

Your treating team and your general practitioner (GP) understand that this is a difficult time and are there to support you. They can set up a mental health plan and refer you to someone to talk to, like a psychologist or counsellor. This can help you to express how you feel, work through those emotions, and learn about coping strategies and relaxation tools that may help you.

It can also be helpful to remember the people, practices and tools that helped you in the first stage of your treatment pathway and use these to help again.

Myeloma Australia can help provide information and support at any time through our Telephone Support Line, Information and Support Groups, seminars and social media platforms.

It can be especially helpful to connect with the myeloma community at a time when things are changing, and you have decisions to make. Remember that you don't need to go through this alone.

> *I had to find a purpose each day after learning my myeloma had relapsed. I gained strength from the friends I've made at my local support group who really understand what I'm going through.*
>
> *My daily Tai Chi exercises are also a good outlet for me and help me cope with the next round of treatment.*
>
> **- Paul, Western Australia**

Communicating with family and friends

Family and friends will want to understand what is happening with your myeloma and know how they can support you. But when you are coming to terms with a relapse and busy starting a new treatment, their well-meaning interest can sometimes feel overwhelming.

Family and friends may struggle to understand that your myeloma has relapsed and was not cured after your first treatment, or that it has become resistant to a treatment, and they may need support themselves. You may like to share this booklet with your family and friends to help them understand.

It can also be helpful to set up a group chat to communicate with loved ones or to nominate a spokesperson to relay information for you. This can help to reduce the stress of needing to answer lots of questions and repeat similar information to different people.

> *I felt disappointed for Barry on learning his myeloma had returned after all the hard work he had put into fighting his disease. His determination gives me strength to continue supporting him to the best of my abilities.*
>
> - Rosemary, carer and wife, Victoria

Final notes

Living with myeloma can at times feel like a rollercoaster ride. There will be ups and downs, but you are not alone.

We hope the information in this booklet has helped you better understand how myeloma behaves and has given you an understanding of what might come in the future.

Myeloma Australia is here to support you, your family, carers and friends. You can stay connected with us by subscribing to receive information and updates on our website:

www.myeloma.org.au

Our specialist Myeloma Support Nurses can be contacted via the details on the next page.

Where to find more information and support

There are many different organisations that can provide you with more information and support:

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

Cancer Council Australia
www.cancer.org.au

Leukaemia Foundation
www.leukaemia.org.au

International Myeloma Foundation
www.myeloma.org

Myeloma UK
www.myeloma.org.uk

Australian Cancer Trials
www.australiancancertrials.gov.au

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

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

Australian Amyloidosis Network
www.amyloidosis.net.au

Australian Department of Human Services
www.humanservices.gov.au
(for information on Medicare and government payments)

Carers Australia
www.carersaustralia.com.au

Carers Couch
www.carerscouch.com

Kidney Health Australia
www.kidney.org.au

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

EviQ Cancer Treatments online
www.eviq.org.au

NPS Medicine Wise
www.nps.org.au

My Aged Care
www.myagedcare.gov.au

Myeloma Australia

This booklet was funded through a non-restrictive grant from Janssen.

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Your tax deductible donation will make a positive impact for people living with myeloma