



Myeloma
Australia

TESTS INFOSHEET

Understanding paraprotein in myeloma


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This infosheet tells you more about paraprotein: what it is, and how it is measured to monitor your myeloma and its response to treatment.

Things to remember

- **Paraprotein is an abnormal antibody, also called an immunoglobulin.** In myeloma, abnormal plasma cells can produce large amounts of a single immunoglobulin called *paraprotein* (or *M-protein*). Most people with MGUS, smouldering myeloma, or active myeloma will produce a paraprotein.
- **Healthy antibodies protect you – paraprotein doesn't.** Normal plasma cells make a mix of antibodies to fight infection. Paraprotein has no useful immune function and very high levels can cause health problems.
- **Paraprotein can be detected in blood and/or urine (wee).** It's one important way your team monitors your myeloma and its response to treatment. They will also check your kappa and lambda light chains and how they relate to each other.
- **Your myeloma type is named after the immunoglobulin produced.** For example, IgG kappa is common. There are also non-heavy chain types – light chain, biclonal, oligosecretory, or non-secretory myeloma – which may need different monitoring.
- **Paraprotein levels are checked regularly.** Your results are compared with those from before treatment and at key points to measure your response to treatment.
- **Trends matter more than single results.** Small changes are common, so your doctor looks at the overall pattern – along with other tests, symptoms, and how you're feeling.

If you're reading a printed version of this infosheet, we've used a magnifying glass symbol  throughout to let you know where you can search for more information in the '**Learn more**' section at the end of this infosheet.

What are plasma cells and immunoglobulins?

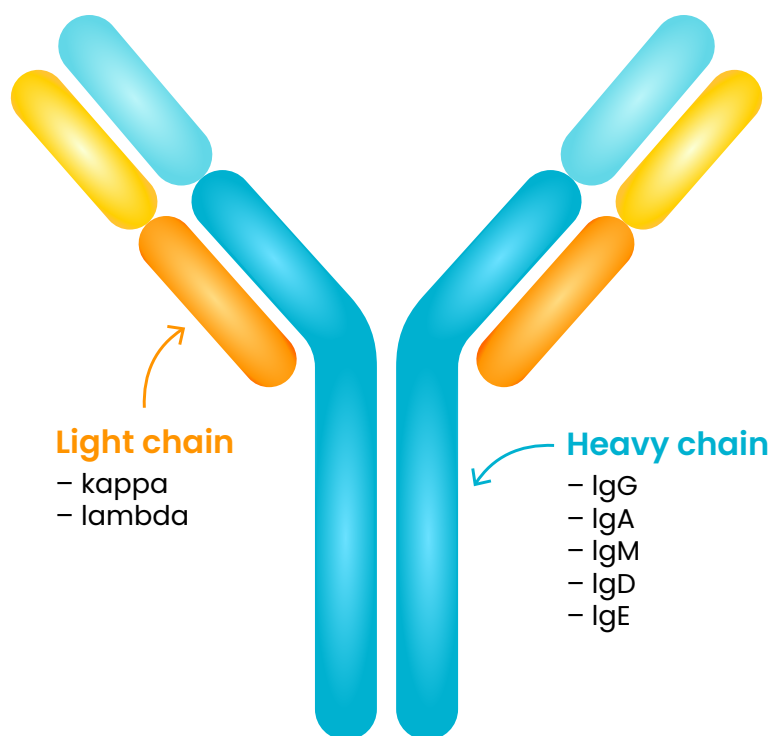
Before we talk about paraproteins, it's helpful to understand plasma cells and immunoglobulins.

Plasma cells are a type of white blood cell found in your bone marrow (the spongy centre of your bones), where they form part of your immune system. Healthy plasma cells make *immunoglobulins* (which are also called *antibodies*), to help fight infection and disease.

When a bacteria or virus enters your body, these immunoglobulins attach (bind) to a protein on the surface of the bacteria or virus. The protein that they bind to is called an *antigen*. This attachment then signals other immune cells to destroy the bacteria or virus, allowing your body to overcome infection.

Immunoglobulins, which are written as 'Ig' for short, are shaped like a Y and have two parts:

1. **Heavy chains:** There are five types: IgG, IgA, IgM, IgD, and IgE.
2. **Light chains:** There are two types: kappa or lambda.



The image above shows the Y shape of immunoglobulins and their heavy and light chains.

Each immunoglobulin has one type of heavy chain and one type of light chain, and each plays a different role in protecting your body against infection and disease.

HEAVY CHAIN TYPE	ROLE IN THE IMMUNE SYSTEM
IgG	IgG attaches to a bacteria or virus that enters your body and signals the immune system to destroy it before an infection develops.
IgA	IgA is found in your mucous membranes (protective layers of tissue that line organs throughout your body). It is the first to detect a bacteria or virus in these tissues.
IgM	IgM is the first immunoglobulin produced in response to an infection.
IgD	IgD's role is not well understood, but is thought to help IgM.
IgE	IgE is responsible for allergic reactions.



LIGHT CHAIN TYPE	ROLE IN THE IMMUNE SYSTEM
Kappa and lambda	Your body creates a unique immunoglobulin for each bacteria or virus it is targeting. For example, the Ig that targets measles is different from the Ig that targets influenza. Light chains are the part of the immunoglobulin that help attach it to a bacteria or virus.

Healthy plasma cells produce a combination of the different types of immunoglobulins, allowing your immune system to fight off a variety of infections. These different combinations of immunoglobulins are called *polyclonal* (meaning many).

What role do plasma cells and immunoglobulins play in myeloma?

Myeloma is a cancer of the plasma cells. When plasma cells become cancerous, instead of producing a combination of the different types of immunoglobulins (polyclonal), they start to produce large amounts of one type of abnormal immunoglobulin (called monoclonal, meaning 'one').

This abnormal immunoglobulin can be found and measured in your blood and/or urine (wee) and is called *paraprotein* or *M protein*. This paraprotein doesn't have any useful function in your body, and at very high levels, can become harmful to your body.

Most people with [monoclonal gammopathy of undetermined significance \(MGUS\)](#) , [smouldering myeloma \(SMM\)](#) , or active myeloma, will produce a paraprotein that can be detected in their blood and/or urine:

- The test used to detect paraprotein in the blood is called *serum protein electrophoresis*, or SPEP for short.
- The test used to detect paraprotein in the urine is called *urine protein electrophoresis*, or UPEP for short.

Your doctor will also look at the balance (ratio) between your two light chains: kappa and lambda. Healthy plasma cells produce an

even balance between the levels of kappa and lambda light chains. Myeloma cells produce too much of one type of light chain: either kappa or lambda. The ‘involved’ light chain makes the balance between the two uneven. Unlike paraproteins, everyone will have some light chains in their blood. Light chains need to be monitored when they are increased above normal levels, and when the balance is uneven.

Types of myeloma

There are different types of myeloma which are named after the type of abnormal immunoglobulin (paraprotein) being made by the myeloma cell.

TYPE OF MYELOMA	FEATURES	EXAMPLE
Heavy chain myeloma	This can be IgG, IgA, IgM, IgD, or IgE myeloma, depending on which heavy chain is producing a paraprotein + either the light chain kappa or lambda.	A common heavy chain type is called IgG kappa myeloma .
Light chain myeloma (also called Bence Jones myeloma)	This is when kappa or lambda light chains break away from the heavy chain and start to be produced on their own. These are called free light chains or Bence Jones protein.	A common light chain type is called lambda light chain myeloma .
Biclonal myeloma (also called double myeloma)	This happens when the myeloma cells start to produce two different types of paraprotein.	A type of biclonal myeloma is when IgG kappa and IgA lambda paraprotein are produced by the myeloma cells.
Oligosecretory myeloma	This is when myeloma cells produce very small amounts of paraprotein that can't be detected on standard blood or urine tests.	This is a single type of myeloma that is always called oligosecretory myeloma .
Non-secretory myeloma	This is when myeloma cells produce no paraprotein that we can detect in the blood or urine, making it more difficult to diagnose and monitor.	This is a single type of myeloma that is always called non-secretory myeloma .

How is paraprotein used to monitor heavy chain types of myeloma?

Measuring the paraprotein level in your blood or urine is the easiest way to monitor all the heavy chain types of myeloma. When myeloma is becoming more active, there is an increase in the paraprotein level. When myeloma is responding to treatment, there is a decrease in the paraprotein level.

It is important to know that a small increase in paraprotein does not always mean you need treatment straight away. It is normal for your paraprotein level to increase and decrease slightly. Sometimes, something as simple as how much fluid you drank before your blood test or having a mild infection can affect blood test results. Your doctor will closely monitor the pattern of your paraprotein level over time.

Your paraprotein result can also differ slightly if your blood and/or urine tests are done at different laboratories. We recommend having your tests done with the same pathology service each time for the most consistent results.

Your paraprotein level will be checked regularly (such as every month or every three months) to see how well your treatment is working, and to check that your myeloma remains stable between treatments.

Paraprotein is only one part of the myeloma picture. Your doctor will also be monitoring other blood test results and checking for any symptoms you may have.

How will my myeloma be monitored if I have a non-heavy chain type?

Biclonal myeloma

Biclonal myeloma is also monitored by detecting paraprotein in your blood and/or urine, but your doctor will test and monitor both types of paraprotein being produced by the myeloma cells.

Light chain myeloma

If you have light chain myeloma (also called Bence Jones myeloma), your doctor will monitor your myeloma using a blood test called *serum free light chain* (sFLC). This blood test measures the amount of free light chains in your blood and their balance (ratio).


When your myeloma is active, there will be an increase in the involved free light chain and a decrease in the uninvolved free light chain, causing the balance to become uneven.

When your myeloma is responding to treatment, there will be a decrease in the involved free light chain level and the balance between the two light chains starts to become even again.

Free light chains are small enough to pass through the kidneys and can be found in your urine. They can also get stuck in your kidneys where they can cause damage. You may need to do a 24-hour urine collection at different times to monitor your free light chain levels. This test is done by collecting your urine at home over a 24-hour period in a container provided by the pathology lab.

Non-secretory or oligosecretory myeloma



If you have non-secretory myeloma, it means the myeloma cells do not produce paraprotein, so we cannot use blood or urine tests to monitor it. This means your myeloma needs to be monitored with more regular bone marrow biopsies or scans instead.

If you have oligosecretory myeloma, you may be able to be monitored using the serum free light chain blood test (sFLC) that is used to monitor light chain myeloma. In some cases, this is not possible, and like people with non-secretory myeloma, your myeloma may need to be monitored with more regular [bone marrow biopsies](#) or scans instead. 

Assessing your response to treatment

Paraprotein levels are used to measure your response to treatment and are usually checked after you finish each cycle of treatment.

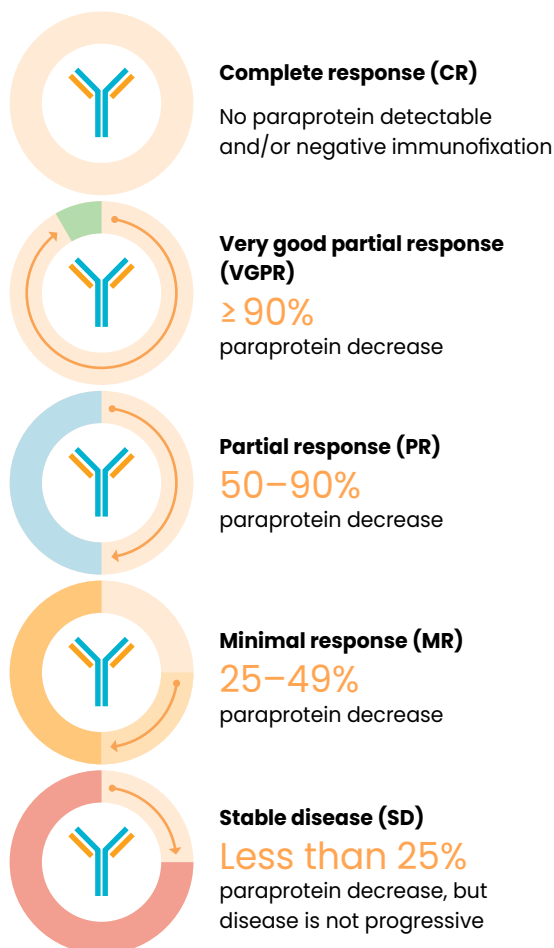
Your doctor will use the *International Myeloma Working Group's Response Criteria* to measure your level of response. This criteria looks at:

- the number of plasma cells in your [bone marrow](#) 
- the level of paraprotein in your blood and/or urine
- the difference between involved and uninvolved free light chain levels
- the presence of [myeloma bone disease](#). 

Your doctor will compare your results from before you started treatment and then at certain points throughout treatment to measure your level of response. Your doctor may also refer to this as your 'depth' of response. It is possible for your myeloma to become active again without producing a paraprotein. This is why it's so important to report any new symptoms to your treating team.

The image to the right shows the different levels of response based on the percentage of paraprotein found after treatment. Remember that if you have light chain, non-secretory or oligosecretory myeloma, your doctor will use different tests to measure your response to treatment.

Different responses to treatment



Other conditions that may produce paraprotein

Having a paraprotein in the blood is not always caused by MGUS, smouldering myeloma, or active myeloma.







Some other conditions that can produce a paraprotein include:

- **Monoclonal gammopathy of renal significance (MGRS)** – a condition that can cause serious kidney damage.
- **Waldenström's macroglobulinaemia** – a rare type of lymphoma (a different blood cancer) that causes a rise in the IgM immunoglobulin.
- **Light chain amyloidosis (AL amyloid)** – a condition where the light chains break away from the heavy chains, change their shape and get stuck in tissues such as the nerves, heart and kidneys. Amyloidosis can happen on its own or together with myeloma.



Learn more


You'll find more information in these Myeloma Australia resources available from myeloma.org.au.


RESOURCE	NAME	LINK
INFOSHEETS	→  'Monoclonal gammopathy of undetermined significance (MGUS) infosheet'	Go to: myeloma.org.au Search for the document using the name following the  icons
	→  'Smouldering myeloma' infosheet'	
	→  'Managing myeloma bone disease' infosheet'	
	→  'Understanding the bone marrow biopsy procedure in myeloma' infosheet'	
	→  'Understanding bone marrow tests in myeloma' infosheet'	

More information and support

→ **Our Specialist Myeloma Nurses** are available on our Telephone Support Line to talk with you about your myeloma treatment and tests, and any questions you have.

To book a 30- or 60-minute call with a Specialist Myeloma Nurse:

 call **1800 MYELOMA** (1800 693 566)
Monday–Friday, 9am–5pm AEST/AEDT, or

 go to **myeloma.org.au** and click on the
'Book a call with a Specialist Myeloma Nurse' button.

 email nurses@myeloma.org.au to contact a Specialist Myeloma Nurse at any time.

We hope this infosheet has helped you understand more about paraprotein and its role in myeloma. Remember to ask your treating team if you have any questions about how your paraprotein and/or free light chains are being monitored, and what the results mean for you.



The information in this sheet is not intended to replace medical care or the advice of your treating team. Please talk to your team about the monitoring and management plan they recommend for you.