

# MGUS

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## Related conditions Infosheet

**This Infosheet explains what Monoclonal Gammopathy of Undetermined Significance (MGUS) is and how it is diagnosed and managed.**

### What is MGUS?

**Monoclonal gammopathy of undetermined significance**, or 'MGUS', is a haematological condition (involving the blood). It is a benign (non-cancerous) condition.

MGUS is characterised by the presence of an abnormal antibody (or immunoglobulin) in the blood and/or urine produced by abnormal plasma cells in the bone marrow.

MGUS does not cause any symptoms and is usually diagnosed incidentally when tests are performed to investigate other problems. It does not require any treatment.

### Plasma cells and the bone marrow

Bone marrow is the spongy centre of bones where blood cells are made. This includes a type of white blood cell called plasma cells. Plasma cells help fight infection by producing antibodies.

## Antibodies

Antibodies are Y shaped and made up of four parts – two identical heavy chains and two identical light chains (see Figure 1).

There are five types of heavy chain: G, A, D, E and M. There are two types of light chain: kappa ( $\kappa$ ) and lambda ( $\lambda$ ).

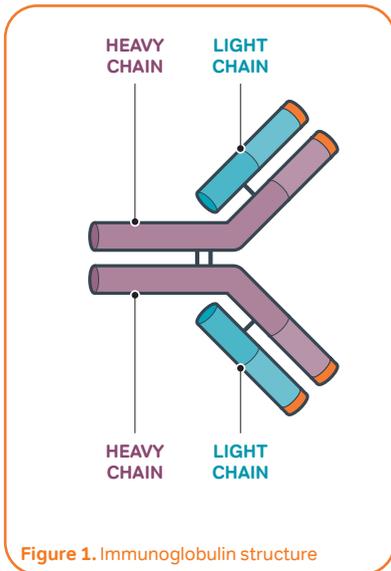


Figure 1. Immunoglobulin structure

## Paraprotein

In MGUS, plasma cells in the bone marrow become abnormal and release an increased amount of a single type of antibody. This is known as paraprotein and it has no useful function.

Paraprotein can also be called M protein, monoclonal protein or abnormal protein. (This protein is not related to dietary protein in any way.)

## Types of MGUS

MGUS can be categorised on the basis of the type of abnormal antibody produced. The categories of MGUS are:

- IgM-MGUS
- Non-IgM MGUS – i.e. IgG, IgA, IgD or IgE MGUS
- Light chain MGUS – where only the light chain part of the antibody is produced and the heavy chains are not

## Who can develop MGUS?

MGUS is a common condition that increases with age. About one in 30 people aged 50 years or older will have the condition, rising to one in 20 people aged over 70 years, and to nearly one in 10 people aged over 85 years. It is about 1.5 times more common in men than in women.

The condition also appears to be nearly twice as common in people of African origin as Caucasian origin.

About four out of five people with MGUS will never know that they have the condition because it usually does not cause any symptoms or lead to a more serious diagnosis.

### **What causes MGUS?**

The exact cause or causes of MGUS are not yet known but is thought to involve complex changes at the genetic level.

### **What are the symptoms of MGUS?**

There are no symptoms associated with MGUS and it does not require treatment. Generally, any symptoms that MGUS patients have are associated with other medical problems.

### **How is MGUS diagnosed?**

As MGUS is not associated with any symptoms, the paraprotein is usually discovered when tests are being performed to rule out other health issues, for example kidney problems, osteoporosis or an inflammatory disorder; or it can be detected during routine pre-operative tests.

Once paraprotein is discovered, it is important to make sure that it is not due to a more serious diagnosis and so further tests are likely to be carried out.

In MGUS, blood and/or urine tests will show:

- A paraprotein level in the blood of 30g/L or less
- Little or no protein in the urine
- A normal calcium level
- Normal kidney function
- No anaemia

If a bone marrow biopsy or X-rays are carried out they will show:

- Less than 10% abnormal plasma cells in the bone marrow
- No bone damage

Some MGUS patients may have an abnormal result for one or more of these tests due to an unrelated condition. For example, it may be possible to have MGUS with anaemia caused by iron deficiency.

### **Can MGUS develop into another condition?**

While most MGUS patients have a stable condition that has no effect on their general health, a very small proportion of patients will go on to

develop a more serious condition, such as myeloma, AL amyloidosis or lymphoma.

MGUS patients will be monitored, usually for the rest of their lifetime, to catch any progression at the earliest possible stage.

MGUS patients should look out for any new symptoms that might indicate the development of a more serious condition.

## Myeloma

Myeloma, also known as multiple myeloma, is a type of blood cancer arising from plasma cells in the bone marrow.

MGUS resembles myeloma due to the presence of abnormal plasma cells in the bone marrow and paraprotein in the blood and/or urine, but at much lower levels than in myeloma.

Unlike MGUS, myeloma causes symptoms and requires treatment.

For more information see [Myeloma – An introduction](#) from Myeloma UK

## Will MGUS develop into myeloma?

The vast majority of MGUS patients do not develop myeloma. Only a small percentage of MGUS patients will go on to develop myeloma –

each year around one in 100 MGUS patients will be diagnosed with myeloma and will need treatment.

Some patients may develop an intermediate condition called smouldering myeloma. This is when the abnormal plasma cells are becoming more active but are not causing the same level of symptoms and complications as in myeloma.

However, it is important to remember that MGUS usually remains stable for many years without progressing to myeloma.

## Is there any way to tell if MGUS will develop into myeloma?

It is not yet clear why only a small minority of patients progress to myeloma and, unfortunately, there is no definitive test to show who will progress to myeloma and who will remain stable long-term.

However, research does point towards certain factors that are associated with an increased risk of progression:

- An abnormal serum free light chain ratio – this is a measure of the ratio between the two different types of light chain (kappa and lambda) that can be produced. An abnormal ratio

shows that there is an increase in the production of one type of light chain

- Non-IgG MGUS
- Higher paraprotein level ( $\geq 15$  g/L)

The more of these factors present, the higher the risk of developing myeloma, although the risk still remains very low. This affects how closely MGUS patients are monitored.

The cause of the progression from MGUS to myeloma is unknown but probably involves further changes at the genetic level. This is an area of active research.

It is important that MGUS patients are vigilant about any new symptoms that may indicate their MGUS is progressing, such as bone pain, kidney damage, fatigue and recurring infection, and report them to their doctor as soon as possible.

### **IgM MGUS**

IgM MGUS is where the paraprotein produced is of the IgM type. This type of MGUS is different from other types, as it can, although rarely, progress to a low grade non-Hodgkin lymphoma (Waldenström's macroglobulinaemia) rather than to myeloma.

Non-Hodgkin lymphoma is a different blood cancer from myeloma and presents with fatigue, anaemia, swollen glands and, sometimes, sweats at night.

### **How is MGUS managed?**

Current guidance recommends that MGUS is actively monitored via blood tests but not treated. MGUS patients are usually checked 6–12 months after diagnosis. The checks are then usually reduced to every 12 months as long as no symptoms develop.

If you have low risk MGUS with no risk factors, your haematologist may discharge you given that the risk of progressing to myeloma is very low. Some patients may be monitored by their GP.

Paraprotein levels can rise and fall in MGUS – this is normal. However, any steady increase in paraprotein level, or development of symptoms, requires further tests to investigate whether MGUS has progressed to myeloma or another condition.

### **Living with MGUS**

For the majority patients, their diagnosis of MGUS has no effect on their daily life. However, it can be concerning to receive a diagnosis

for which there is no treatment and has the (very small) possibility of developing into another condition.

You can be reassured that your healthcare team will monitor you for any signs of progression and will take action as appropriate. If you are concerned, you should speak to them in the first instance. You can also call the [Myeloma Infoline](tel:08009803332) on [0800 980 3332](tel:08009803332) to speak to one of the Myeloma Information Specialists at Myeloma UK.

## Summary

- Monoclonal gammopathy of undetermined significance (MGUS) is a non-cancerous (benign) condition
- MGUS is where abnormal plasma cells in the bone marrow produce a useless antibody (immunoglobulin) called paraprotein
- There are no symptoms and no treatment for MGUS
- In a very small number of cases, MGUS can develop into other conditions, such as myeloma
- Patients with MGUS will be monitored

## About this Infosheet

The information in this Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation.

For a list of references used to develop our resources, visit [myeloma.org.uk/references](https://myeloma.org.uk/references)

We value your feedback about our patient information. For a short online survey go to [myeloma.org.uk/pifeedback](https://myeloma.org.uk/pifeedback) or email comments to [myelomauk@myeloma.org.uk](mailto:myelomauk@myeloma.org.uk)

## Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management, and related conditions. Download or order them from [myeloma.org.uk/publications](https://myeloma.org.uk/publications)

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma Infoline on **0800 980 3332** or **1800 937 773** from Ireland.



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Get in touch to find out more about how we can support you

Call the Myeloma Infoline on

 **0800 980 3332**

Email Ask the Nurse at

 **AskTheNurse@myeloma.org.uk**

Visit our website at

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