Waldenstrom's Macroglobulinaemia and Lymphoplasmacytic Lymphoma:

A guide to treatments

0300 373 8500 | support@wmuk.org.uk | wmuk.org.uk

This guide was made possible by the generosity of the WM and LPL community and its supporters.

If you have any questions about any aspect of WM and LPL – including symptoms, treatments and help available – visit our website: **wmuk.org.uk**, contact our Support Line on 0300 373 8500 or email us at **support@wmuk.org.uk**

Contents

About This Guide

This guide has been created specifically for those living with Waldenstrom's macroglobulinaemia (WM) and lymphoplasmacytic lymphoma (LPL) and for their friends and family.

This guide will help you understand:

- What treatments are available
- How to prepare for treatment
- What to expect from each type of treatment
- How to cope with treatment and side effects
- Where you can find out more information

It's important to remember that everyone's experience of WM and LPL is different. Many patients may be treated for conditions they develop that are related to their WM or LPL diagnosis. You can read more about this in our **Related Conditions Booklet.**

If you need more in-depth information about WM or LPL or want further details about the support available to you, and your family and friends, just go to our **Other Resources Section on page 58**, where you'll find useful links and contact numbers – including our free WMUK Support Line: **0300 373 8500.**

A few notes

- This guide has been created for you in consultation with expert healthcare professionals and people living with WM or LPL. However, it can only give general guidance and should not replace the personalised advice and care given to you by your healthcare team.
- All the information in this guide is intended for people living and being treated in the UK, so some information may not be accurate for those living abroad.
- Your healthcare team may use drugs not mentioned in this booklet.
- While we hope you find this helpful, it is not a replacement for the national and international guidance from healthcare authorities.

If you or someone close to you has recently been diagnosed with WM or LPL, you may like to read this section on our website:

www.wmuk.org.uk/your-journey-with-wm/newly-diagnosed-with-waldenstrom-macroglobulinaemia/

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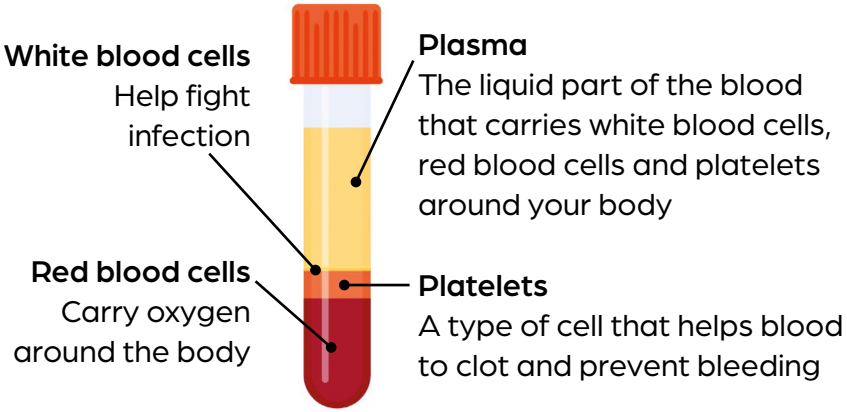
What Are WM and LPL ?

Waldenstrom's macroglobulinaemia (WM) and lymphoplasmacytic lymphoma (LPL) are rare types of blood cancer.

- They are forms of blood cancer called lymphoma, belonging to a group of cancers known as 'Non-Hodgkin Lymphomas.'
- They aren't curable at the moment, but there are many effective treatments that can help with symptoms, address any complications, and help extend the periods between treatments.
- Because WM and LPL are slow-growing, they don't always need treating right away.
- Symptoms can vary from person to person.

What Causes WM and LPL?

Your blood is made up of different parts: red blood cells, white blood cells, platelets, and plasma. These cells are made inside your bones, in what's known as your bone marrow. Sometimes, the process goes wrong and the cells develop incorrectly, or abnormally.



In people with WM or LPL, a type of white blood cell called B cells (or B lymphocytes) develop abnormally. These abnormal B cells do not work properly, but they continue to be produced and build up in the bone marrow. As they increase in number, they crowd out healthy blood cells, stopping them from doing their jobs. This causes many of the symptoms seen in WM and LPL.

What is the Difference Between LPL and WM?

Waldenstrom's macroglobulinaemia (WM) is a type of lymphoplasmacytic lymphoma.

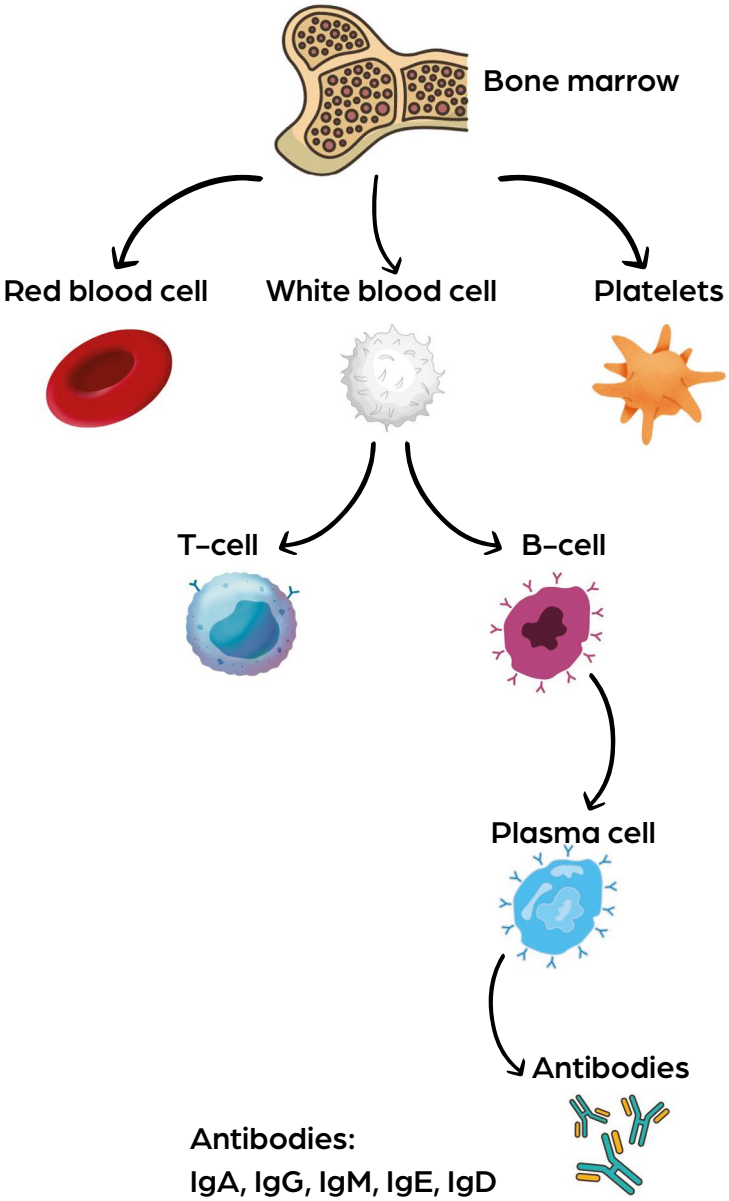
If you have WM, your B cells make too much of a certain protein called IgM. This can make your blood thicker than normal, which may cause symptoms like headaches or vision problems.

Not everyone with LPL has WM. For people without WM, their abnormal B cells produce a different abnormal protein (usually IgG or IgA) or no proteins at all. They may be told that they have Non-IgM LPL, or Non-WM LPL.

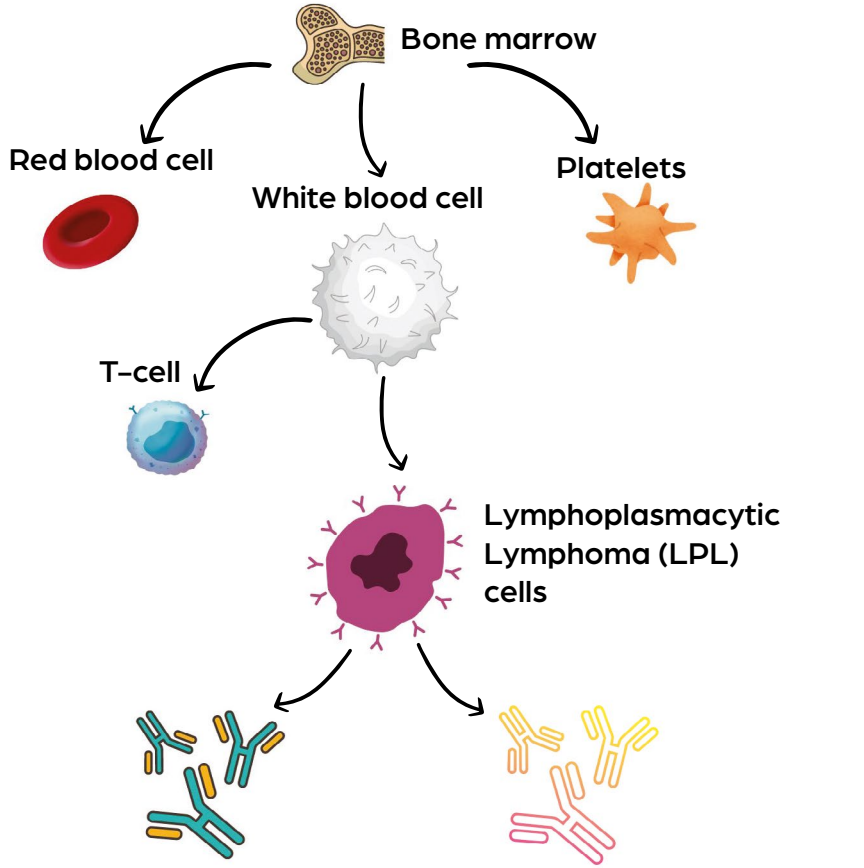
19 out of 20 people with LPL have WM.

The latest guidelines say that treatment used for WM and non-IgM LPL should be the same.

Normal Blood Cell Production

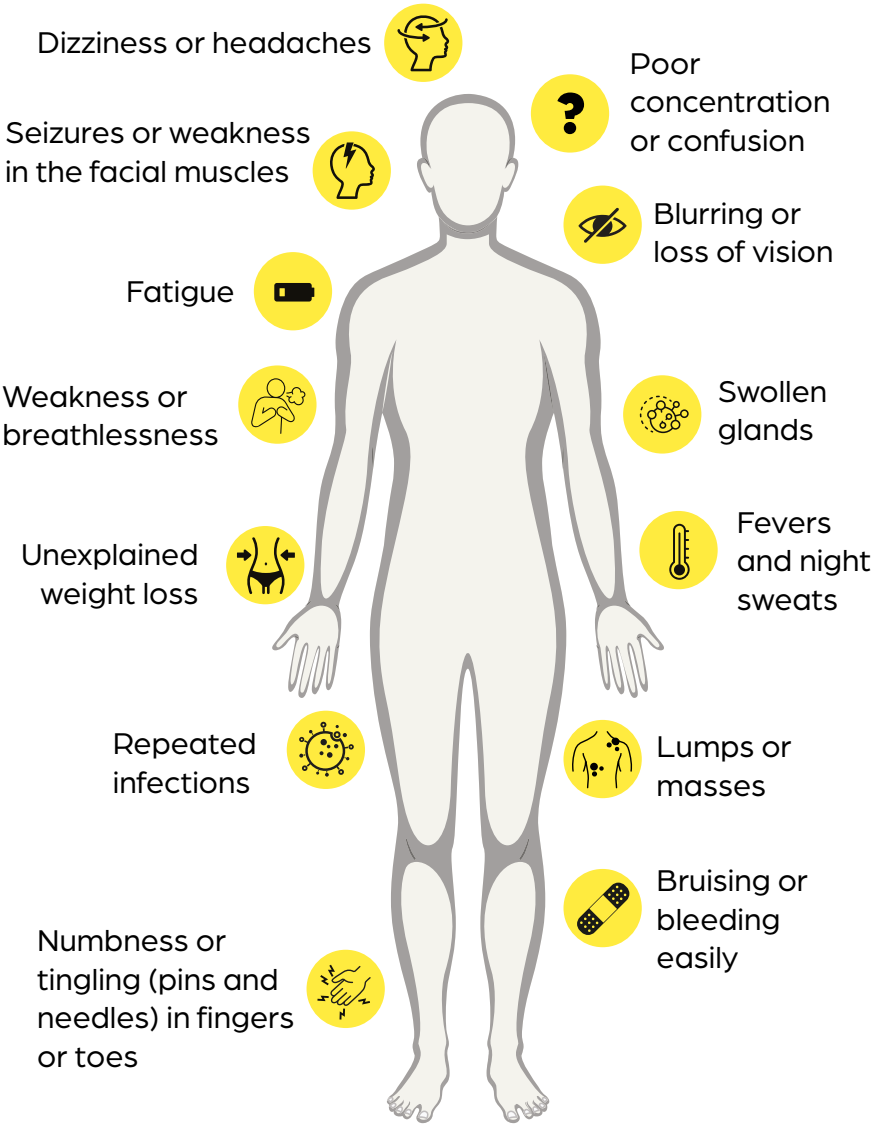


Blood Cell Production in WM and LPL



Understanding Symptoms

Those living with WM and LPL may experience a range of symptoms. It's important to be aware of symptoms and let your healthcare team know, so they can monitor or make changes to your care.



Active Monitoring

Before you start treatment, many people with WM and LPL will be supported through 'active monitoring'. This is when your healthcare team will keep track of your symptoms and check the levels of abnormal antibodies (paraprotein), produced by the abnormal B cells, in your blood along with other factors.

There is no evidence that starting treatment earlier has any benefits for patients. The side effects of some treatments can be harsh, so doctors wait until the benefits of treating WM and LPL outweigh the negative side effects people might get with the treatment. Some people may be on active monitoring for years.

What happens during active monitoring?

When you're first diagnosed with WM or LPL, if you are not treated, check-ups may be once every 3 months. If your WM or LPL is stable and you don't have any symptoms, you may have check-ups every 6 months or even just once a year. But if your health ever changes, or you get any symptoms, you can contact your healthcare team and they will provide advice and see you sooner if needed.

WM and LPL are slow-growing cancers so you may not start treatment immediately after your diagnosis.

During your check-ups, you'll have the opportunity to share your experiences and any concerns you have about your health with your medical team. It's important to mention any symptoms at these check-ups, no matter how small.

Your symptoms may indicate that you are ready for treatment; they could be the result of a condition related to WM; or you could be offered treatment to help manage the symptom rather than treat the cancer itself.

You can find more information about active monitoring on our website

www.wmuk.org.uk/your-journey-with-wm/active-monitoring-wmuk

Starting Treatment

The results of your blood tests together with the symptoms you have will help your doctor to decide if it's time to start treatment. Most symptoms are caused when abnormal B cells (WM and LPL cancer cells) crowd out the other healthy cells and prevent them from doing their job.

For example, the abnormal cells might take up the space of healthy red blood cells, which carry oxygen around your body. When you don't have enough of these cells, you develop anaemia which can make you feel overly tired and short of breath.

When your platelets are affected by the abnormal WM or LPL cells, you might find you start bruising more easily, or even start bleeding from your nose, gums or elsewhere. Your healthcare team will consider a number of things before they suggest treatments, these will include:

- Your age
- Your general health
- Your fitness
- Your symptoms
- Any conditions you may have that are related to WM and LPL, such as neuropathy or Bing–Neel Syndrome. (You can read more about these in our Related Conditions Booklet)
- Any treatment you've had before and how your body responded

The Goal of Treatment

There are many different treatments. Some can help to control symptoms and side effects that the cancer may cause, while others attack the cancer (abnormal B cells) directly. It is common to receive a combination of both.

Ultimately, the aim of WM and LPL treatment is to send the disease into what is known as 'remission'. This is when the cells that cause WM or LPL have been reduced, leading to a reduction or improvement in your WM or LPL symptoms. This might help you to feel better than before you went on treatment.

Treatment Overview

Your healthcare team will advise you on the treatments that are best for you, taking into consideration your symptoms and other factors. Sometimes you'll be put on a treatment regimen which is a plan that may involve a single drug or combination of drugs.

The team will usually provide you with other medications to take throughout the cycle, to help you manage the specific side effects of the treatment or reduce your risk of infection.

Treatment cycles vary in length depending on what drugs you are taking. The drugs used can have side effects or be harsh on your body, so the cycles are planned to give your body time to recover and the blood counts to come back up, ready for the next round.

Your first course of treatment is called a 'first-line' treatment. The usual first-line treatment is chemo-immunotherapy (which aims to kill the abnormal B cells) but your healthcare team will talk through the options that best suit you.

Over time, the abnormal B cells in your body may start to increase again, which will be identified through changes in symptoms or through blood tests. If they do, you might need a second, or even third, course of treatment. These courses are known as 'second-line' and 'third-line'.

These treatments might be chemotherapy, but there are also other options, such as non-chemotherapy, targeted treatments like BTK inhibitors and, in some individuals, stem cell transplants.

Symptom Treatment		Page
Antibiotics	Kill the germs which cause infections.	19
Plasma exchange	Treats symptoms by reducing the thickness of the blood.	21
Steroids	Control symptoms or fight cancer in combination with other treatments.	23
WM and LPL Treatment		
Chemotherapy	Kills the cancer cells.	25
Monoclonal antibodies	Kill cancer cells and help your body's immune system to kill the cancer.	29
BTK (Bruton's tyrosine kinase) inhibitors	Control the number of B cells in the blood.	31
Chemo–immunotherapy	Kill the cancer cells and help your body's immune system to kill the cancer.	33
Less Common Treatment		
Stem Cell Transplant	Uses very high doses of chemotherapy to try to kill as many cancer cells in the body as possible. The bone marrow is then replaced with healthier stem cells to make new blood cells.	42
CAR T-cell therapy	Kill cancer cells.	46
R-CHOP or R-Pola-CHP	Combination of drugs used if WM/LPL transforms into a more aggressive lymphoma.	48

Symptom Treatment

Antibiotics

People with WM and LPL have a weaker immune system making them more likely to get infections. This happens when the WM and LPL cancer cells (abnormal B cells) crowd out healthy white blood cells, weakening your immune system.

If you are given treatment, such as chemo-immunotherapy, this can also reduce the number of white blood cells in your body, making it harder to fight infection.

If you're undergoing treatment that doctors know will put you at risk of infection, they may give you antibiotics beforehand, as a preventative measure. Antibiotics may also be used to treat infections including those caused by other conditions that are related to WM and LPL.

How long does treatment take?

How long you need to take antibiotics for will depend on a number of factors. Patients who are given preventative antibiotics may need to take them for the duration of their treatment, and for a few months after.

If a patient develops an infection, then a short course of antibiotics may be required for 7 to 14 days, depending on the severity. In some cases, patients with frequent infections or who have a particularly poor immune system, may be prescribed long-term antibiotics that could be taken for months or even longer.

What are the side effects?

Occasionally, people have an allergic reaction to antibiotics. In most cases, it will be mild and can be successfully treated by taking antihistamines. Side effects may include:

- A raised, itchy skin rash
- Coughing
- Wheezing
- Tightness of the throat and difficulties breathing

NOTE:
For information on managing side effects see page 51.

Plasma exchange

In patients with WM (and less commonly those with non-IgM LPL) cancer cells produce excessive amounts of the protein IgM, which builds up in the plasma and can cause the blood to become thick and sticky, a condition also known as hyperviscosity.

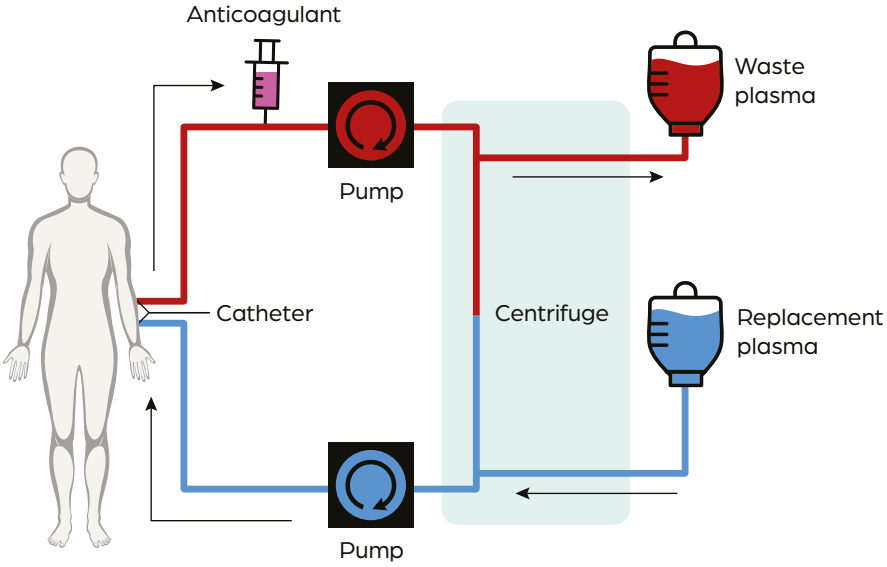
Plasma exchange (also called plasmapheresis) involves your blood being drawn into a machine which removes the IgM and swaps it with a harmless replacement fluid. It usually takes between 1 and 3 exchanges for your symptoms to reduce and the thickness of your blood to return to safer levels.

The aim of the treatment is to make your blood less thick and sticky. If your blood is too thick or sticky it can cause hyperviscosity syndrome (HVS), which can be very dangerous. HVS can increase the risk of a blockage in the blood vessels making it hard for blood to get to your vital organs, such as your heart, brain, liver, and kidneys. It can also increase the risk of bleeding in organs such as the back of the eye or from the gums or nose.

What happens during treatment?

During plasma exchange, blood is removed from your body using a needle put into a vein – similar to the ones used when people donate blood. The blood is then passed through a plastic tube and into a machine which separates the harmful thick plasma from the healthy parts of your blood. Plasma is then replaced with a thinner fluid, before it is transferred back into your body. Each session will last about 90 minutes.

How Therapeutic Plasma Exchange works



How many rounds of treatment will I need?

Some people may need a plasma exchange to quickly reduce high levels of the abnormal protein in the blood and relieve symptoms. It is usually carried out over 1–3 consecutive days and may be given before treatment starts, alongside treatment, or occasionally on its own. In some cases, it may need to be repeated 4–8 weeks later, particularly while treatment begins to reduce the number of cancer cells producing the abnormal protein.

What are the side effects?

Everyone responds differently to treatment. Most side effects last for a short period of time and can be easily managed. Some side effects could include:

- Low blood pressure (hypotension)
- Fatigue or weakness
- Calcium loss and muscle cramps
- Infection or bleeding risk (from the catheter)
- Allergic reactions to replacement fluids
- Nausea or feeling cold

NOTE:
For information on managing side effects see page 51.

Steroids

Your body naturally produces hormones called steroids. They play an important role in regulating your blood pressure and fighting infection. Your doctor may offer you man-made steroids as part of your treatment. The steroids dexamethasone, prednisolone, hydrocortisone and methylprednisolone are most commonly used by those with WM and LPL.

Steroids can be used to address a number of issues. They can help reduce inflammation in the bone marrow, nerves, blood vessels or other tissue. Sometimes the immune system can become overactive and damage healthy cells, so steroids may be used to slow down activity to prevent damage.

They can also prevent an allergic reaction to cancer and reduce sickness that some patients experience. Steroids also kill cancer cells and help the chemotherapy drugs to do their job.

What happens during treatment?

Steroids are often given as tablets. If you are given tablets to swallow, take them with a meal or some milk because they can irritate your stomach. Sometimes they're given as an IV infusion through a drip.

How long does treatment last?

Depending on why you are taking them, you may be given steroids before, during or after cancer treatment.

What are the side effects?

Everyone responds differently to treatments. The severity of side effects will depend on the dosage and how long you have been taking the steroids. Some side effects could include:

- Weight gain
- Increased appetite
- Mood swings
- Difficulty sleeping
- High blood sugar
- Weakened bones (osteoporosis)
- Increased risk of infections
- Fluid retention
- A puffy face
- Thin skin that bruises easily
- Potential eye problems like cataracts

NOTE:

For information on managing side effects see page 51.

WM and LPL Treatment

Chemotherapy

Chemotherapy uses a type of drug or combination of drugs that target and destroy the cancer cells (abnormal B cells) that prevent the healthy white blood cells from working in patients with WM or LPL. This also reduces the production of excess amounts of the IgM protein (or IgG/IgA in non–IgM LPL).

When treating WM and LPL, chemotherapy is often combined with a type of drug known as a monoclonal antibody, such as rituximab, which helps the body's own immune system to fight the cancer cells too. The other name for this combination is chemo–immunotherapy.

For patients with WM and LPL, the combinations of chemotherapy which are used are known as DRC and BR. [For more info, turn to the chemo–immunotherapy section on page 33].

It can take several months after chemotherapy for abnormal protein levels to fall, although they may continue to improve even after treatment has finished. The treatment you receive will depend on your symptoms and how well your body is able to tolerate the drugs.

What happens during treatment?

Different chemotherapy drugs are given in different ways. You may swallow tablets, have an injection or receive the treatment straight into the bloodstream through something called an intravenous infusion (or IV). IVs can be given in a few different ways:

- The drugs can be given via a small thin tube (called a cannula) that goes into a vein in your arm. A new cannula is put into a vein every time you have the infusion treatment.
- The drugs can also be given via a more permanent tube which goes directly into one of the large blood vessels in your chest. This tube (called a central venous catheter, shortened to CVC) will stay in place until you have finished the course of treatment. The CVC will either sit at the top of your arm, on the chest wall or, very rarely, in your neck. The treatment is given through this and bloods can often be taken out of this. There are a few different types of CVC:

  - **PICC line (Peripherally Inserted Central Catheter) –** the line goes into a vein in your arm.
  - **Hickman line –** is inserted into one of your veins in the neck or under the collar bone.
  - **Portacath –** is a small device implanted under the skin, usually on the chest.
  - **Central line –** is a long, flexible tube inserted into a large vein in the chest, neck, or arm.

Most people don't need to stay in hospital during their chemotherapy treatment. If you're having chemotherapy intravenously, you will be treated as an outpatient in a specialist clinic or infusion centre by specialist nurses.

You might just have one drug, or you may have more than one at a time. This is called combination therapy or, depending on the drugs used, chemo–immunotherapy (see page 33 for more information).

Common types of chemotherapy

Bendamustine

Bendamustine is usually given as an intravenous infusion (IV) and each treatment will take between 30 minutes and an hour.

Before you start bendamustine, you will have some blood tests to make sure that your kidneys and liver are healthy and to check the amount of different blood cells and other substances in your blood. You'll also have regular checks throughout the course of your treatment.

Cyclophosphamide

Cyclophosphamide may be given on its own, or in combination with other chemotherapy drugs. It can either be given as an intravenous infusion (IV) drip into your bloodstream or as tablets. If you are given cyclophosphamide tablets to take, you need to swallow them whole with plenty of water. It is important that you take the exact dose that has been prescribed for you. If you miss a dose, contact your healthcare team as soon as possible.

Less common chemotherapy

Chlorambucil

Chlorambucil is a type of oral chemotherapy medication called an alkylating agent, that kills the cancer cells by targeting their DNA. It is sometimes used if patients are older or very frail.

How long does chemotherapy treatment take?

A course of chemotherapy usually lasts between 3 to 6 months, although it can vary. The frequency of each cycle, and length of each treatment course, depends on many factors including the:

- Type of drugs that you're taking
- Side effects the drugs might cause
- Time you'll need to recover from side effects

What are the side effects?

Side effects will vary from person to person and will depend on many factors. While you're having chemotherapy, you'll be at a higher risk of infection. This is because while chemotherapy targets the cancer cells, it also kills some of the other healthy white blood cells which are part of your immune system. Doctors will help you identify the signs of infection, so they can treat you as quickly as possible.

If your white blood cell count becomes very low, you may need to have a blood transfusion or delay your next chemotherapy session. You may also be given injections to boost your white blood cells.

Other side effects may include:

- Fatigue
- Difficulty concentrating
- Disrupted sleep patterns
- Sore mouth
- Change or loss of appetite
- Sickness
- Diarrhoea
- Constipation

NOTE:
For information on managing side effects see page 51.

Monoclonal antibody therapies

Monoclonal antibodies help your body's immune system to kill cancer cells. Rituximab is one of the most common drugs used to treat WM and LPL. It sticks to the cancer cells so that your immune system knows they are harmful and kills them. Rituximab is used in combination with chemotherapy drugs.

Rituximab can have an effect on other parts of your body such as your liver and kidneys. If you have had hepatitis before, rituximab can allow it to reactivate and cause liver problems, so medical teams will check for HIV and hepatitis B and C before prescribing the drug.

What happens during treatment?

Rituximab is given through an intravenous infusion straight into the bloodstream. The first infusion is normally given slowly and the rate is gently increased, as there is a higher risk of a reaction with the first dose.

Rituximab can sometimes cause the abnormal protein in the blood (IgM) to temporarily increase before it improves. If IgM gets too high, the blood can become thicker than normal.

Thick blood can cause symptoms like headaches, dizziness, blurred vision, or shortness of breath. Because of this risk, doctors may skip rituximab during the first few treatment cycles until the protein level is safer.

How long does treatment take?

The infusion will last a few hours, starting slowly to make sure your body doesn't have a reaction to the drug. The speed of the infusion will then be increased. The rituximab will be given more quickly on subsequent visits as your body will be used to it.

What are the side effects?

Some side effects can include heart problems or increase your risk of bleeding, which your health team should talk to you about before you start treatment. Some people have an allergic reaction to monoclonal antibodies that includes:

- Breathlessness or breathing difficulties
- Fever and chills
- An itchy rash
- Flushes and faintness
- Diarrhoea
- Tiredness
- Feeling or being sick
- Headaches

NOTE: Contact your medical team if you have these side effects as they may be able to provide treatment to ease them.

BTK inhibitors

BTK inhibitors, like zanubrutinib and ibrutinib, target a chemical in the body called Bruton's tyrosine kinase (BTK). BTK controls the growth of the cancerous cells (abnormal B cells), and BTK inhibitors stop it working, killing the cancerous cells.

What happens during treatment?

Both zanubrutinib and ibrutinib are given as a daily tablet or tablets. Some people find this more convenient than having IV drugs because you don't have to go to hospital.

How long does treatment take?

Patients will take the treatment for as long as it is working against the WM or LPL, which may be several years. If there are bad side effects, which is uncommon, the treatment is stopped.

What are the side effects?

BTK inhibitors may be less effective in patients who have a particular genetic defect. There may also be some side effects, although most patients don't have serious ones.

They do make the platelets in the blood less sticky (like aspirin does) so people may bruise or bleed more. There is also the chance of high blood pressure and a small risk of an irregular heart rate, called atrial fibrillation (AF), so patients may have a heart scan before starting treatment.

The most common side effects include:

- Tiredness
- Skin rash
- Diarrhoea
- Bleeding or bruising
- Infection

NOTE: It's important to let your healthcare team know if you experience any side effects from the treatment. If you are concerned call 999 immediately.

Chemo-immunotherapy

Chemo-immunotherapy is sometimes known as combination therapy. The chemotherapy kills cancer cells, while the immunotherapy helps your body's defences recognise and attack the cancer cells more effectively.

The most common combinations of treatment are known as DRC (dexamethasone, rituximab, and cyclophosphamide) or BR (bendamustine and rituximab). Your healthcare team will suggest the best option for you based on multiple factors.

A Comparison of DRC and BR Treatment Cycles

Feature	DRC	BR
Total cycles	Usually 6	Usually 4–6
Cycle length	Around 21 days	Around 28 days
Treatment days per cycle	5 days (oral cyclophosphamide + IV treatment)	2 days IV (sometimes 2–3 days if rituximab doses are split)
Home medication	Yes (oral cyclophosphamide)	No
Rituximab timing	Every cycle on day 1	Usually on day 1 of each cycle (sometimes split over 2 days)
Overall intensity	More spread out	Shorter, more intensive IV days

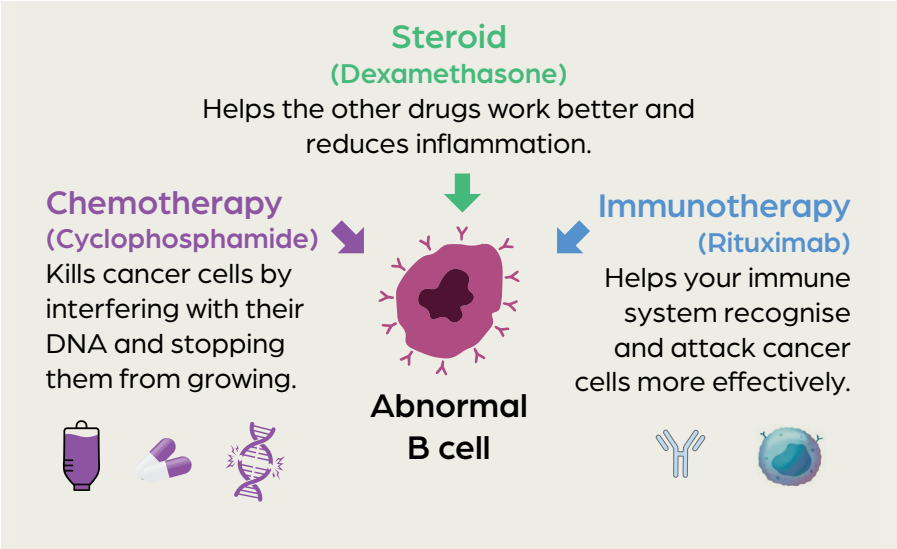
NOTE: The table above outlines a general treatment schedule, though this may vary depending on your individual circumstances. Your healthcare team will be able to advise on what is best for you.

What is DRC?

DRC includes a combination of the drugs dexamethasone, rituximab, and cyclophosphamide.

How chemo–immunotherapy works

Chemo–immunotherapy (combination therapy) uses three types of treatment that work together to fight cancer.



Together this combination of drugs help to treat WM and LPL in different but complementary ways.

DRC includes a combination of dexamethosone, rituximab and cyclophosphamide

Drug	Type	What it does
Dexamethasone	Steroid (read more about it on page 23)	Helps reduce inflammation and can make treatment more effective
Rituximab	Monoclonal antibody (read more about it on page 29)	Helps the immune system target cancer cells and destroy them
Cyclophosphamide	Chemotherapy known as an alkylating agent, that kills the cancer cells by interfering with their DNA (read more about it on page 27)	Damages cancer cell DNA, preventing them from growing and dividing

How long does the treatment take?

Usually there are 6 treatment cycles of DRC, each one lasting 21 days. Most people are given dexamethasone and rituximab on the first day of each cycle. Rituximab is given as an intravenous infusion along with the dexamethasone as an injection or tablet. Usually two tablets of cyclophosphamide are taken for the first five days of each treatment cycle.

You will have a blood test before the treatment to check the level of IgM protein in your blood. If your IgM or blood

thickness is too high, the dose of rituximab will be delayed until your IgM goes down.

Cycle length: 21 days
Total cycles: Usually 6 cycles
Total duration: Around 18 weeks (about 4–5 months)

What to expect from a DRC Treatment Cycle

Day 1

- Blood test (including IgM level check)
- If IgM is too high → rituximab may be delayed
- Premedication:
  - Paracetamol
  - Antihistamine (e.g. chlorphenamine)
  - Steroid cover
- Treatment:
  - Rituximab IV infusion
  - Dexamethasone (tablet or injection)

Days 1–5

- Cyclophosphamide tablets (usually for 5 days)

Days 6–21

- Rest period / recovery
- Monitoring for side effects and blood counts

NOTE: This may vary depending on your individual circumstances. Your healthcare team will be able to advise on what is best for you.

What are the side effects?

Some people have a reaction to the intravenous infusion used for the rituximab. There are also risks of infections during and after chemo–immunotherapy. On very rare occasions, individuals develop a severe skin reaction and a very small risk of a serious brain infection.

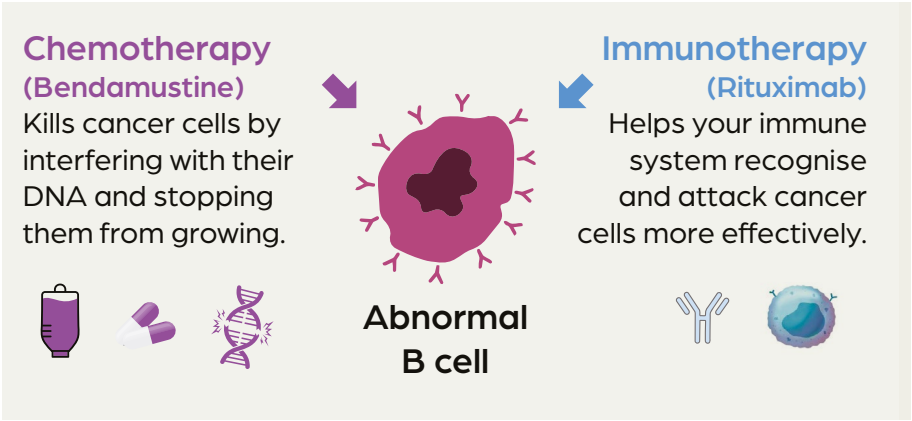
Patients who are on rituximab will be given additional drugs before each dose of the treatment to prevent an allergic reaction. This will include paracetamol, a steroid and an antihistamine drug such as chlorphenamine (Piriton).

What is BR?

BR includes a combination of the drugs bendamustine and rituximab.

How chemo–immunotherapy works

Chemo–immunotherapy (combination therapy) uses two different types of treatment that work together to fight cancer.



Together this combination helps treat WM and LPL in different but complementary ways.

Drug	Type	What it does
Bendamustine	Chemotherapy known as an alkylating agent, that kills the cancer cells by interfering with their DNA (read more about it on page 27)	Damages cancer cell DNA, preventing them from growing and dividing
Rituximab	Monoclonal antibody (read more about it on page 29)	Helps the immune system target cancer cells and destroy them

How long does treatment take?

Most patients having BR will have between 4 and 6 treatment cycles, each usually lasting two days. Rituximab is usually given only on the first day of each treatment cycle.

Bendamustine is usually given on the first and second day of each cycle. Sometimes the second day of bendamustine may be skipped if your doctor decides to reduce the dose to make treatment safer and easier for you to tolerate.

Cycle length: Usually 28 days (varies by hospital)
Total cycles: 4–6 cycles
Total duration: About 4–6 months

What to expect from a BR Treatment Cycle

Day 1

- Blood test (including IgM level check)
- If IgM is too high → rituximab may be delayed
- Premedication:
  - Paracetamol
  - Antihistamine (e.g. chlorphenamine)
  - Steroid cover
- Treatment:
  - Rituximab IV infusion
  - Bendamustine IV infusion

Day 2

- Bendamustine IV infusion (second dose, which may be missed depending on the body's reaction)

Days 3–28

- Recovery period
- Blood monitoring
- No routine chemotherapy unless adjusted

NOTE: This may vary depending on your individual circumstances. Your healthcare team will be able to advise on what is best for you.

What are the side effects?

Some people have a reaction to the intravenous infusion used to deliver the rituximab. Those who are on rituximab will be given additional drugs before each dose of the treatment to prevent an allergic reaction. This will include paracetamol, a steroid and an antihistamine drug such as chlorphenamine (Piriton).

There are also risks of infections during and after chemo-immunotherapy, and on very rare occasions a severe skin reaction, brain infection or sepsis. Sepsis occurs when the level of white blood cells drops very low. Symptoms include feeling extremely unwell, struggling to pass urine, feeling sick, having a high fever, and shivering as your body temperature drops.

Less Common Treatment

Stem cell transplants

A stem cell transplant is a treatment used after strong chemotherapy, which can damage healthy bone marrow as well as cancer cells. Stem cells are the cells in your bone marrow (the runny bit in the middle of your bones) that make new blood cells. A transplant replaces damaged stem cells with healthy ones so your body can start making blood cells again.

It is an intensive procedure that is only offered as a second- or third-line treatment. It usually involves a long hospital stay and can cause serious side effects, and recovery may take many months.

What happens during treatment?

During a stem cell transplant, very high doses of chemotherapy are given to destroy any remaining cancer cells that may still be in the body after a course of chemotherapy.

Stem cells that were collected before the transplant are infused back into the patient. These stem cells replace the damaged bone marrow and 'rescue' the patient's blood cell production.

Although a stem cell transplant is not a cure, it can lead to longer-lasting remission, which means the cancer is controlled for a longer period of time.

A stem cell transplant will not be offered until other treatments have been tried and will only be considered if you are in good physical health.

Types of stem cell transplant

Autologous transplants

Autologous transplants involve transferring your own stem cells, that are collected or 'harvested' after your main chemotherapy course, back into your body. These stem cells help your body recover and make new blood cells.

While the chemotherapy will have killed many of the cancer cells, some that survive may be mixed in with your harvested stem cells that are transferred back into your body. This means that even though things get much better, the cancer will usually come back at a later date, but remission should last longer than it would with chemotherapy alone.

Allogeneic transplants

Allogeneic transplants use stem cells from another person (a donor). Following chemotherapy the donor's healthy stem cells will be transferred to replace a patient's old cells.

The donor's immune cells can also attack and destroy leftover cancer cells, which gives extra protection.

This type of transplant can be more effective as the new cells help fight the cancer too. However, it is a much harsher treatment than the autologous transplant as the donor's stem cells may recognise the patient's own body cells and attack them. The patient will therefore need anti-rejection medicines to reduce these side effects.

What are the stages of treatment?

A stem cell or bone marrow transplant is a long and complicated process that involves five main stages.

These stages are:

- **Tests and examinations –** to assess your general health.
- **Harvesting –** collecting stem cells to use in the transplant, either from you or a donor. There are different ways of collecting stem cells that include:
  - **From blood –** stem cells are removed from the blood using a special machine.
  - **From bone marrow –** a sample of bone marrow is removed from the hip bone.
  - **From cord blood –** blood from the placenta and umbilical cord of a newborn baby is used as the source of stem cells.
- **Conditioning –** A high dose of chemotherapy and sometimes radiotherapy is used to kill all the remaining cancer cells, or as many as possible, after the previous chemotherapy courses.

- **Transplanting the stem cells –** This is usually done a day or two after conditioning has finished. The stem cells are given through a drip into a vein (an intravenous infusion), which usually takes a few hours.

  The new stem cells travel to the bone marrow and start making healthy blood cells again. This helps your body recover and fight infection.

  In an allogeneic transplant (using donor stem cells), patients may also receive anti-rejection drugs to stop their immune system from rejecting the donor cells.

- **Recovery –** Patients need to stay in hospital for a few weeks or even a few months. During this time their blood cell count will be very low and they'll be at high risk of infection. They usually require platelet and blood transfusions. When the transplanted stem cells start to produce enough new blood cells the body starts to recover and a patient will be allowed home.

How long does treatment take?

Treatment and recovery can take up to a year. Stem cell transplants aren't done in all NHS hospitals, so you may be referred to a specialist centre. This could mean a lot of travel, depending on where you live.

What are the side effects?

Stem cell transplants are very intensive and physically demanding and aren't suitable for everyone. There are also some serious side effects that mean that the treatment is too risky for some people. Some side effects include:

- Nausea and vomiting
- Indigestion
- Heart burn
- Diarrhoea and constipation
- Mouth sores
- Low blood cell counts
- Infections
- Bleeding
- Skin and hair problems
- Fatigue

The following additional side effects are usually only seen in those who have allogeneic transplants from other people.

- Veno-occlusive disease (VOD)
- Pain in your nerves, bones, joints, and other organs.
- Graft-versus-host disease which occurs when the donor's stem cells attack the recipient's cells.

NOTE:
For information on managing side effects see page 51.

CAR T-cell therapy

Chimeric Antigen Receptor T-cell therapy (CAR-T therapy) is a new type of treatment. T-cells are a type of white blood cell found in the body. They are important as they help your body fight infections. During CAR-T therapy, the T-cells are removed, modified and put back into your blood stream so that they can find the cancer cells and kill them with the help of the rest of the immune system.

This therapy is quite new and not given to people with WM or LPL unless part of a clinical trial.

What happens during treatment?

T-cells are collected from the patient's blood and sent to a laboratory to be modified. The new cells are then given back to the patient through an IV drip, similar to a blood transfusion. The new modified T-cells recognise the WM or LPL cancer cells, stick to them, and help the immune system kill them.

There are a lot of tests to have before receiving CAR T-cell therapy and only a small number of specialised hospitals in the UK provide the treatment.

How long does the treatment take?

CAR-T therapy typically takes several weeks to complete. While the process of transferring the modified cells back to a patient takes less than an hour, most patients will need to be monitored in hospital for several days to a couple of weeks depending on their situation.

What are the side effects?

This treatment can be effective, but it can cause very serious side effects. People who have CAR T-cell therapy are not allowed to drive, operate heavy machinery, or do any other dangerous activities for at least a few weeks after treatment.

NOTE:
For information on managing side effects see page 51.

R-CHOP or R-Pola-CHP

R-CHOP or R-Pola-CHP are treatments that are used if someone gets what is called 'transformed lymphoma.' This is when the cancer becomes more aggressive, which is very rare and happens in around 5-10% of patients.

R-CHOP includes a combination of 5 drugs: rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone.

Pola-R-CHP includes the following: polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisolone.

There is more detailed information about this on the WMUK website

www.wmuk.org.uk/your-journey-with-wm/when-waldenstroms-macroglobulinaemia-comes-back/

Keeping Well and Coping with Treatment

It's important to look after yourself both physically and mentally before, during and after treatment. Before you start treatment, think about some things to help make it easier for you and those around you.

- **Getting to and from appointments**
  You might not be able to drive yourself. If you don't have anyone you can call upon, ask your healthcare team if they are able to help with transport.
- **Work**
  You may not be able to work for a while after treatment and you might need to take time off for tests before the treatment starts. Talk to your employer as soon as possible. You can find some useful information about working when you have WM or LPL on our website.
- **Finances**
  You might be eligible for some financial support, especially if you need to take a long break from work. A social worker will be able to help with advice.

- **Childcare**
  If you have children, ensure you have someone who can help you look after them whilst you are having treatment.
- **Pet care**
  If you need to spend time in hospital, you'll also need to make arrangements for any pets to be cared for.
- **Household chores**
  It is important to keep your home clean, to help prevent infections. If possible, try to find someone who can help with housework whilst you are having treatment.
- **Avoiding Infections**
  It's important to avoid getting an infection while on treatment. Try to keep your home clean and avoid crowded places. Stay away from anyone with an infection, a cold, cough, and illnesses like chicken pox that spread easily. You should also watch out for signs of infection and let the hospital know immediately if you feel unwell so you can get the right treatment.
- **Vaccinations**
  Staying up to date with your vaccinations can help protect you from infection. However, if you have been diagnosed with WM or LPL, it's generally advised to avoid 'live' vaccines, as these contain a small amount of the virus or bacteria they protect against. Speak with your medical team about which vaccines are recommended for you and the best time in your treatment cycle to receive them.

Managing Side Effects

Everyone experiences different side effects. It's important to keep an eye on these and let your healthcare team know, as they can suggest ways to help relieve the symptoms.

Some side effects are more serious and could be an indication that you have sepsis. If you experience these symptoms, you should seek emergency medical care immediately or call 999.

Sepsis can be life-threatening and needs urgent treatment. Contact your hospital team immediately or go to the emergency department if you:

- **feel suddenly very unwell**
- **stop passing urine or pass much less urine than usual**
- **have a high temperature or start shivering**
- **feel sick or are vomiting**
- **become confused, drowsy, or difficult to wake**

Family or friends may notice that you seem confused or are not acting normally. If this happens, seek urgent medical attention straight away.

Supporting Medication

Alongside your treatment, you may also be prescribed additional medications to help prevent side effects or reduce the risk of complications. These may include:

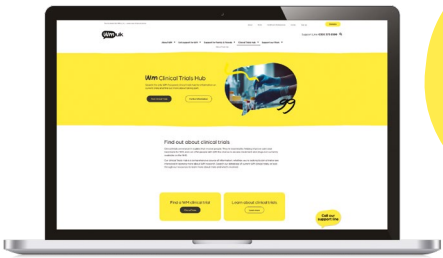
- **Steroids** to improve the effectiveness of treatment and help prevent side effects, such as nausea. They can also increase appetite and reduce any inflammation. (See more on page 23)
- **Aciclovir** to help prevent viral infections, such as shingles.
- **Co-trimoxazole** to reduce the risk of certain bacterial and fungal infections.
- **Allopurinol** to help protect your kidneys by reducing uric acid levels when treatment is started.

Clinical Trials

Clinical trials are essential to helping improve care and treatment for WM and LPL, and can offer those living with the conditions the chance to access treatment and drugs not currently available on the NHS.

Through the WMUK Clinical Trials Hub, you can search directly for clinical trials currently recruiting that you might be eligible for. There's also additional information about what is involved in a clinical trial and how to apply.

If you are interested in taking part in a clinical trial, then make sure you discuss the options with your healthcare teams.



To explore the Clinical Trials Hub, visit wmuk.org.uk/wm-clinical-trials-hub

Finding Support

Being diagnosed with WM or LPL can come with a range of emotions. Sometimes it can be good to speak to people who understand what you're going through, to get advice or just to talk things through.

1–2–1 Support

Speaking to someone on a 1–2–1 basis can really help – whether you have worries, aren't feeling yourself or have questions you wished you'd asked your doctor.

WMUK offers both emotional and clinical support via our Support Line.

The Support Line is staffed by an expert WM/LPL nurse, who is there to help you navigate the world of WM and LPL and can also signpost you to other resources or organisations that may be useful.

You can call the Support Line on: 0300 373 8500. Alternatively, you can get in touch via email anytime on: support@wmuk.org.uk

Support Groups

Even if you have supportive friends and family, sometimes you might feel like they don't understand. Meeting people who are going through a similar experience to you can be a good way to feel less alone. Support Groups do just this, bringing together people with WM and LPL who live in the same region or have similar experiences to share their stories and advice.

To find out more visit: www.wmuk.org.uk/giving-you-support-for-wm/national-support-groups/

Buddy Service

Through our Buddy Service we link those who have been recently diagnosed with WM or LPL or are just starting treatment with another patient who has similar experiences. Many patients find it helps to hear directly from someone who understands firsthand what they are going through.

To find out more visit: wmuk.org.uk/giving-you-support-for-wm/wmuk-buddy-service/

Online Support

You might not feel comfortable talking face-to-face so we also run forums to allow people to chat online.

To find out more visit: www.wmuk.org.uk/giving-you-support-for-wm

Join our Facebook Group

We run a thriving Facebook group for people living with WM and LPL. There you can meet and chat with over 600 people, all at varying stages of their WM and LPL journeys.

You can join here: www.facebook.com/WMUKCharity

Sources and Acknowledgements

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For a full list of the sources used in our WM and LPL information, please email: **info@wmuk.org.uk.**

We welcome all feedback on our resources. If you have thoughts you'd like to share, please email **info@wmuk.org.uk.**

About WMUK

WMUK is the only charity in the UK focused solely on Waldenstrom's macroglobulinaemia (WM) and lymphoplasmacytic lymphoma (LPL). Our vision is that people affected by WM and LPL can live longer, good quality lives, being supported every step of the way by WMUK.

Through working with the WM and LPL community, we build support programmes that help to empower patients and their families so that they can live fulfilled lives. We organise meet-ups, conferences, virtual webinars and run a thriving forum which is a welcoming place for anyone needing a listening ear.

Our website and Support Line are also sources of reliable and accessible information, so that everyone affected by WM and LPL can get the answers and support they need, whenever they need it.

Find out more: wmuk.org.uk

Contact the WMUK Support Line: 0300 373 8500

Email the Support Line: support@wmuk.org.uk

For general enquiries call us on: 0300 303 5870

We're here for **you.**

Other Resources

Related Conditions Guide – A complete overview of the symptoms, diagnosis and treatment for conditions related to WM and LPL.

Newly Diagnosed Booklet – A comprehensive overview of what to expect on your WM and LPL journey and how to live well physically and emotionally after diagnosis.

Visit our website for more in depth information about WM and LPL **www.wmuk.org.uk/your-journey-with-wm**

Call our Support Line anytime: WMUK is always here to support you and those close to you – including family members, friends and carers. You can call or email our Support Line (0300 373 8500 or **support@wmuk.org.uk**) for answers to your questions or simply if you need a listening ear. Our friendly, expert team are always here to help.

Support Groups

Connect with other people living with WM or LPL in your local area:

www.wmuk.org.uk/giving-you-support-for-wm/

Support For Loved Ones

Find advice and support for friends, family and carers on our website:

www.wmuk.org.uk/friends-family-carers-wmuk/

From Other Organisations:

Find out about the emotional support services offered by the Penny Brohn charity: **pennybrohn.org.uk**

Get mental health support from: **mind.org.uk**

Get free expert cancer care and support at a Maggie's Centre near you: **maggies.org**

Trusted Information Creator

Patient Information Forum

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