NCCN GUIDELINES FOR PATIENTS®

2022

Waldenström Macroglobulinemia

Lymphoplasmacytic Lymphoma

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These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma, Version 2.2022 – December 7, 2021.

NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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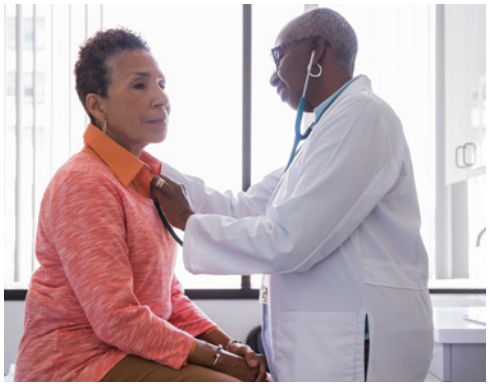



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1
WM basics

Waldenström macroglobulinemia (WM) is a slow-growing cancer that does not always require treatment. It is a type of non-Hodgkin lymphoma called lymphoplasmacytic lymphoma.

What is WM?

Waldenström macroglobulinemia is a non-Hodgkin lymphoma. Non-Hodgkin lymphoma is not a single disease. It refers to a group of many different cancers that start in white blood cells called lymphocytes. Some types are fast-growing (aggressive), while others are slow-growing (indolent). In general, WM grows slowly and does not always require treatment.

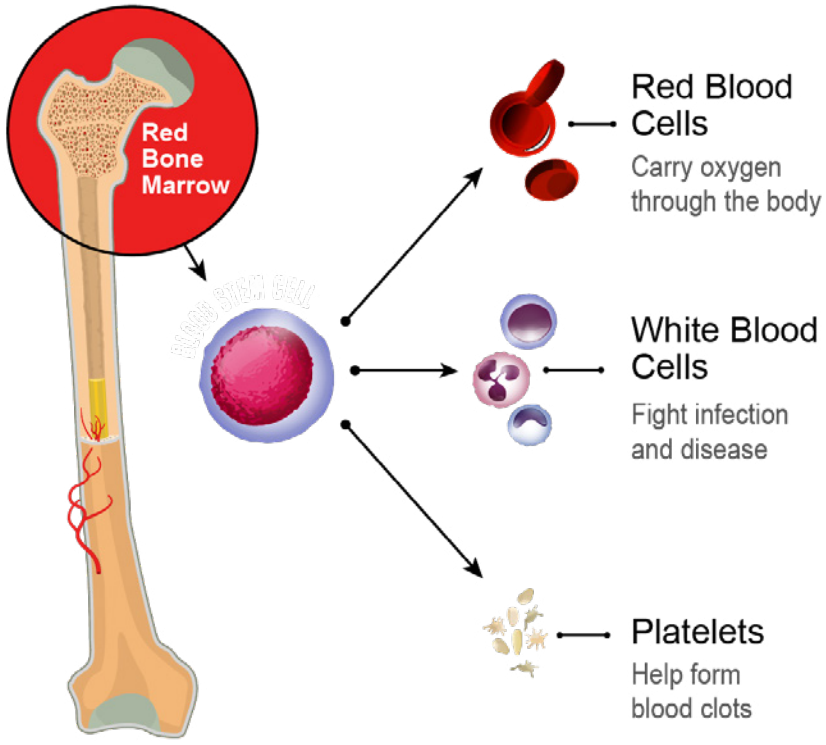
WM is the most common form of lymphoplasmacytic lymphoma (LPL). LPL starts in the bone marrow and can cause a shortage of essential blood cells needed by the body. In WM, a naturally occurring but dysfunctional protein called an antibody is also released into the blood. Large amounts of this antibody can cause blood to become abnormally thick.

How WM starts

Most bones have a soft, spongy filling called bone marrow. Bone marrow is where blood cells are “born” as blood stem cells. Blood stem cells develop into one of three types of “mature” blood cells, which have different jobs in the body.

Blood cells

Bone marrow is where the essential blood cells needed by your body are “born” as blood stem cells. Blood stem cells develop into red blood cells, white blood cells, or platelets.



- White blood cells help the body fight infection
- Red blood cells carry oxygen throughout the body
- Platelets help wounds heal by forming blood clots

The lymphatic system is a network of tissues and organs that help your body fight infection and disease. It is a major part of the body's immune system. The tissues and organs that make up the lymphatic system are made mostly of white blood cells called lymphocytes. The two main types of lymphocytes are B lymphocytes (B cells) and T lymphocytes (T cells).

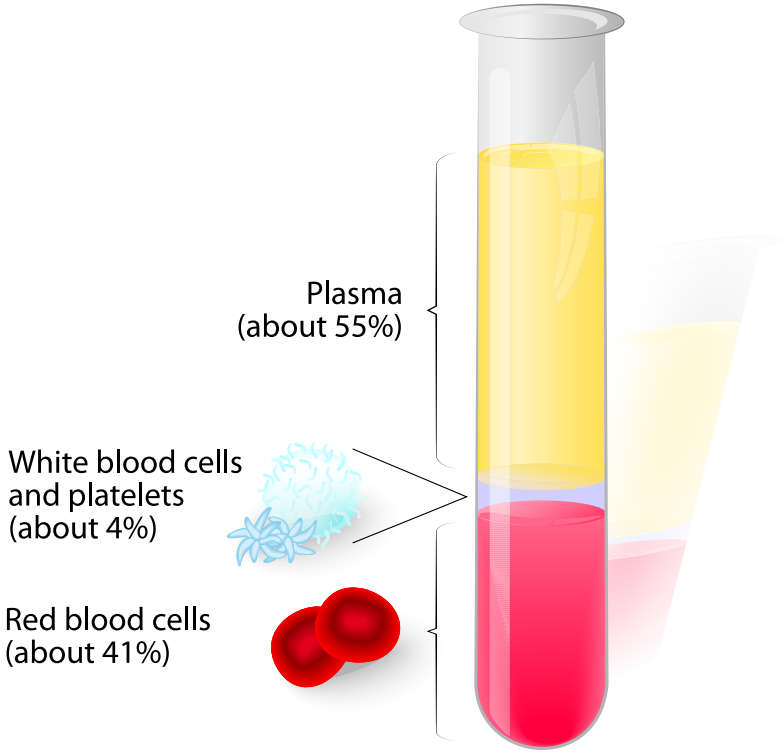
In lymphoplasmacytic lymphoma, B cells can change and start to take on features of a different type of white blood cell called a plasmacyte, or plasma cell. These "hybrid" lymphocyte–plasmacyte cells multiply over and over. The cells eventually take over the bone marrow, preventing it from making the blood cells needed by the body. The shortage of blood cells starts to cause health issues that you can notice (symptoms).

Antigens and antibodies

An antigen is any substance that makes your immune system jump into action to protect itself. In other words, antigens are things your body perceives as non-self or threats. Antigens can come from outside the body, such as toxins, viruses, chemicals, and bacteria. Antigens can also be found inside the body, such as on the surface of cancer cells or other cells.

Structure of blood

Red blood cells, white blood cells, and platelets are carried throughout the body in a clear, yellow liquid called plasma. Plasma makes up a little over half of blood. The antibody that causes blood to thicken in some people with WM is found in plasma.



Antibodies (also called immunoglobulins) are proteins that work in different ways to help your body protect itself against antigens. There are 5 main types of immunoglobulins ("Ig" for short): IgA, IgD, IgE, IgG, and IgM.

Immunoglobulin M (IgM) is the first antibody your body makes to fight a new infection. Most adults have a very low level of IgM in the blood at any given time. In most people with LPL, the cancer cells make and release large amounts of IgM into the blood. This is Waldenström macroglobulinemia (WM).

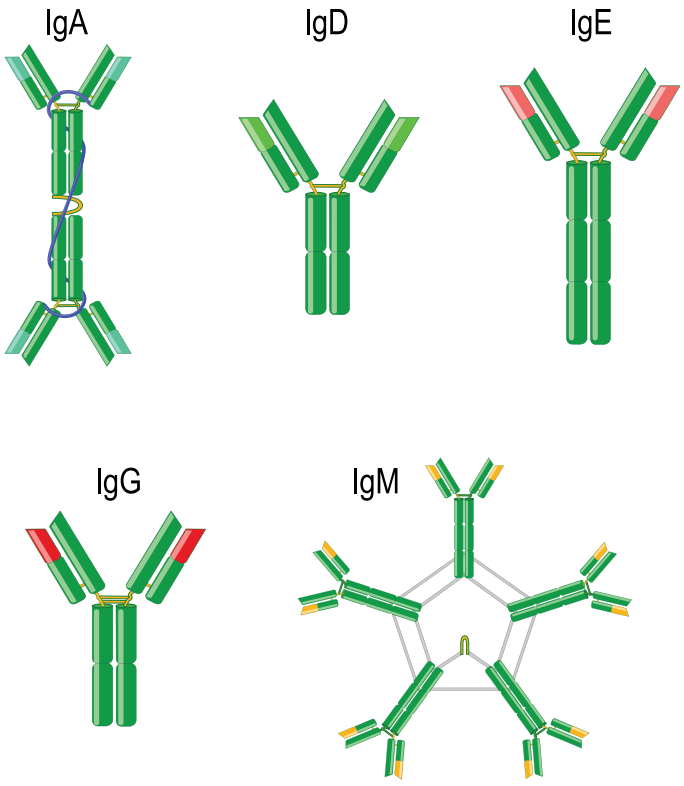
In some people with WM, there is so much IgM in the blood that it becomes abnormally thick. This is called hyperviscosity. Blood cannot flow through the body properly if it is too thick. Hyperviscosity can cause symptoms including abnormal bleeding (especially from the nose and gums) and vision problems (blurred or double vision). Other effects of hyperviscosity include nervous system symptoms (headaches, dizziness, seizures) and cardiovascular symptoms (shortness of breath, chest pain).

Asymptomatic WM

Long before causing any symptoms, WM starts as IgM monoclonal gammopathy of undetermined significance (IgM MGUS). In IgM MGUS, the level of IgM in the blood is higher than normal, but low compared to WM. There is also a low percentage of lymphoplasmacytic cells in bone marrow. If these levels increase but not enough to cause symptoms, it is referred to as "smoldering" or asymptomatic WM. No treatment is needed for IgM MGUS or smoldering WM.

Types of antibodies

IgM is the largest of all the antibodies. Its bulky size and structure contribute to the abnormal thickness of the blood (hyperviscosity) that can be found in some people with WM.



Key points

- WM is a slow-growing cancer that affects the blood and does not always require treatment.
- WM is the most common type of a non-Hodgkin lymphoma called lymphoplasmacytic lymphoma (LPL).
- In WM, the cancer cells make and release large amounts of an antibody called immunoglobulin M (IgM) into the blood.
- In some people with WM, there is so much IgM in the blood that it becomes abnormally thick. This is called hyperviscosity.
- Hyperviscosity can cause dangerous bleeding or clotting problems. They often involve the eyes, gums, and skin.
- Hyperviscosity can also cause vision problems, nervous system symptoms, and cardiovascular (heart and lung) issues.
- No treatment is needed for IgM MGUS or smoldering (asymptomatic) WM.

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Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback

2
Testing for WM

If your doctors suspect WM, one of the first things they will do is test your bone marrow.

Bone marrow tests

A small amount of bone marrow needs to be removed from your body in order to be tested. This is done in two ways:

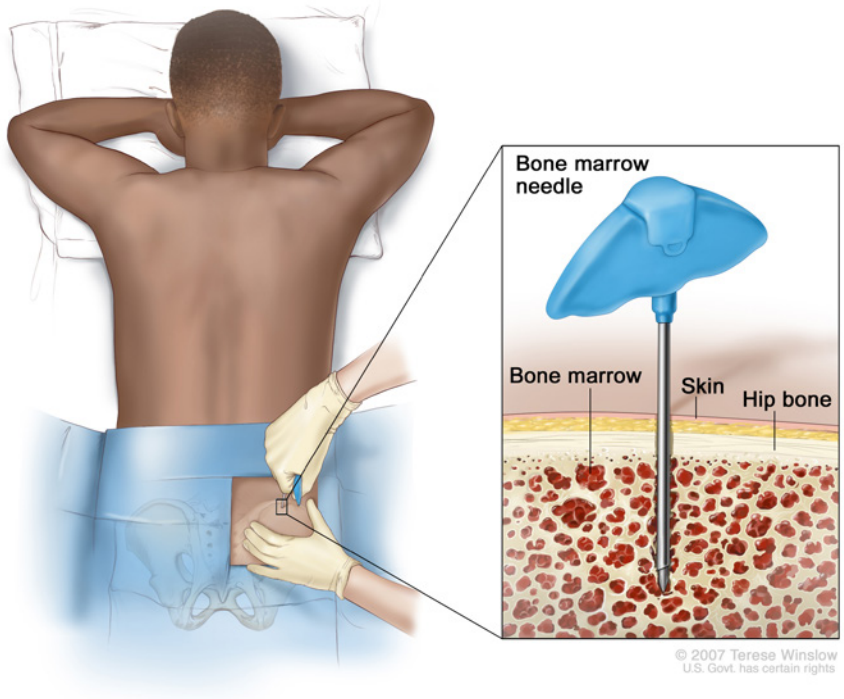
- Bone marrow aspiration removes a small amount of liquid bone marrow.
- Bone marrow biopsy removes a small amount of solid bone and bone marrow.

These procedures are usually done at the same time on the back of the hip bone. Rarely, marrow is removed from the breastbone. You may receive a light sedative before the test. Your doctor will clean your skin and then use local anesthesia to numb the site. Once numb, a hollow needle will be inserted into your skin and then pushed into the bone to remove the liquid bone marrow with a syringe. Then, a slightly wider needle will be inserted into the bone and rotated to remove a small piece of bone and soft marrow. These biopsies may cause bruising and tenderness or pain at the biopsy site. In rare cases, the biopsy may cause a hematoma. A hematoma is a collection of blood under the skin, trapped outside of a blood vessel. It is not the same as a bruise.

The bone marrow samples are sent to a laboratory and tested by an expert in diagnosing diseases of the blood and bone

Bone marrow aspiration and biopsy

In order to diagnose (or rule out) WM, a sample of your bone marrow must be tested. If cells that have features of both B cells and plasma cells can be seen under a microscrope, it is likely that you have WM. You will have other tests to confirm the diagnosis.



marrow, called a hematopathologist. Testing looks for the following things:

- Lymphoplasmacytic cells in your bone marrow
- Proteins usually seen on the surface of lymphoplasmacytic cells
- Gene mutations usually found in people with WM

These tests are explained in greater detail below.

Pathology review

After a biopsy, the removed tissue is sliced into very thin layers that are placed on a glass slide and examined under a microscope. In people with LPL or WM, there are abnormal cells that have features of both lymphocytes and plasma cells. These cells are called lymphoplasmacytic cells.

Protein tests

The removed bone marrow is also examined under a microscope to look for proteins usually found on the surface of WM cells. Proteins called sIgM, CD19, CD20, and CD22 can usually be seen in people with WM, but proteins called CD5, CD10, and CD23 are much less commonly seen. The names of the laboratory tests used to look for these proteins are:

- Flow cytometry
- Immunohistochemistry (IHC)

Genetic testing

Genes are pieces of DNA that contain information passed from parent to child. Humans have over 20,000 genes. Every person has two copies of each gene, one from each parent. Genes contain instructions that determine things like your eye color, hair color, and height.

Genes can undergo changes called variants or mutations. Some mutations are harmful and can increase the risk of developing certain cancers, for example. Other mutations may have health benefits or may not impact your health at all.

Mutations can occur spontaneously or as a result of exposure to harmful things in the environment. Mutations can also be passed down from parent to child (inherited). There are two gene mutations that may be found in people with WM and that may affect treatment planning.

Most people with WM have an abnormal (mutated) version of a gene called *MYD88*. Everyone with suspected WM should be tested for this mutation. While uncommon, it is possible to have WM even if you don't have the *MYD88* mutation.

Blood tests

In addition to bone marrow tests, blood tests play an important role in diagnosing and planning treatment for WM.

Testing for antibodies

People with WM have a high level of an antibody called immunoglobulin M (IgM) in their blood. If WM is suspected, your doctor will order blood tests to determine the types and amounts of antibodies in your blood. The names of these blood tests are:

- Serum quantitative immunoglobulins
- Serum protein electrophoresis (SPEP)
- Serum immunofixation electrophoresis (SIFE)
- Serum free light chain (SFLC)

Blood viscosity test

High levels of IgM in the blood can cause it to thicken. This is called hyperviscosity. A blood (also called serum) viscosity test measures the thickness of blood. Blood thickness is measured in centipoise (cP).

A blood viscosity level of 1.8 cP is considered higher than normal. Symptoms of hyperviscosity often start when the viscosity level goes above 4.0 cP, but some people may have symptoms at a lower level.

Your doctor may order a viscosity test if you have symptoms of hyperviscosity, such as abnormal bleeding, vision problems, or nervous system problems.

Beta-2 microglobulin

Beta-2 microglobulin is a protein that can be measured in blood. The level may be high in people with cancer of the blood or bone marrow. This test may provide information about how severe the cancer is and how it will respond to treatment. More research is needed, however, on using beta-2 microglobulin levels to make treatment decisions.

Complete blood count

One of the most common blood tests is called a complete blood count (CBC). A CBC measures the number of white blood cells, red blood cells, and platelets in the blood. Blood counts are often low in people with WM.

Blood smear

A blood smear is a test that provides information on both the number and shape of blood cells in a sample. It is recommended as part of the initial testing for WM.

Blood-clotting test

If you have unexplained bruising or bleeding, you may be tested for a blood clotting disorder called von Willebrand disease. This disease is rare and most people who have it are born with it. However, it can develop later in life in people with WM and similar diseases, usually in people with a high blood IgM level. If this happens, it is called acquired von Willebrand disease.

Cold-sensitive antibodies

Some people with WM have abnormal antibodies in their blood that react to cold temperatures. These cold-sensitive antibodies

can affect the level of IgM in blood. They may or may not cause symptoms.

Cryoglobulins are one type of cold-sensitive antibody that can be found in people with WM. They can interfere with blood IgM level measurements by causing the level of IgM to be lower than it is.

When the body drops below its normal temperature, cryoglobulins form solid or gel-like clumps that block blood flow to your body. This is called cryoglobulinemia. Over time, this can damage blood vessels and tissues. A test called a cryocrit will be ordered if cryoglobulinemia is suspected.

Cold agglutinins are a less common type of cold-sensitive antibody. Less than 10 percent of people with WM have cold agglutinins in their blood. Antibodies that mistakenly target or harm the body's own tissues or organs are called autoantibodies. Cold agglutinins are autoantibodies that harm red blood cells.

At low temperatures, cold agglutinins cause red blood cells to clump together (agglutinate), which causes the red blood cells to be destroyed by the body. A very high level of cold agglutinins in the blood can cause a serious health condition called chronic hemolytic anemia, in which red blood cells are destroyed faster than they are made.

Hepatitis B

Some targeted therapies used to treat WM can activate the hepatitis B virus in people who are carriers. Being a carrier means you have the hepatitis B virus in your blood, but you do not have any signs or symptoms of the disease. If treatment with certain targeted therapies is planned, expect to be tested for the hepatitis B virus.

If you are a carrier, you will be closely monitored for signs and symptoms of active hepatitis B infection during treatment and for several months afterward. Your doctor may prescribe antiviral medication to prevent re-activation of the hepatitis B virus.

Hepatitis C

People with WM—especially those with cryoglobulinemia—may have underlying hepatitis C. If your doctor suspects that you have cryoglobulinemia, your blood will likely be tested for the hepatitis C virus.

Non-Waldenström lymphoplasmacytic lymphoma

Because Waldenström is the most common form of lymphoplasmacytic lymphoma, the names are often used interchangeably. While there are types of LPL that do not release IgM, these "non-Waldenström" types make up less than 5 percent of all LPLs. Treatment of these rare types of LPL is similar to that of WM, but people with a non-Waldenström LPL are less likely to have hyperviscosity.

Other blood tests

Your doctor will order other blood tests that provide information about how well your liver, kidneys, and other organs are working. The levels of the following will be tested:

- Blood urea nitrogen (BUN) to creatinine ratio
- Electrolytes
- A protein made by the liver called albumin
- Calcium
- Uric acid
- An enzyme called lactate dehydrogenase (LDH)

Imaging

A widely used imaging test called computed tomography (CT) can provide additional information about the extent of WM. CT takes many pictures of an area of the body from different angles using x-rays. A computer combines the x-rays to make detailed pictures.

CT scans of your chest, abdomen, and pelvis are recommended to help your treatment team determine if your lymph nodes, spleen, or other organs are enlarged. CT can also show if cancer has spread beyond the bone marrow.

A substance called contrast is used to make the pictures clearer. The contrast is injected into your vein. You will be asked a series of questions to make sure you are not allergic to the dye. Allergic reactions include throat swelling and hives.

Other testing

Urine tests

IgM can collect in both blood and urine. Your doctor may order one or more of the following tests to gain additional information:

- 24-hour urine for total protein
- Urine protein electrophoresis (UPEP)
- Urine immunofixation electrophoresis (UIFE)

Health history and physical exam

Expect your doctor to review your health history in detail. Your doctor will want to know a lot about your past and current health. You will likely be asked about:

- Illnesses, diseases, and surgeries
- Medicines that you take (prescription or over-the-counter)
- Your lifestyle (your diet, how active you are, and whether you smoke or drink alcohol)
- Symptoms that may be related to WM or complications of WM

Your doctor will also perform a thorough physical exam of your body to look for signs of WM and for general signs of disease.

Retinal exam

Hyperviscosity can cause eyesight problems such as blurred or double vision. If the level of IgM in your blood is 3.0 g/dL or higher, or if your doctor suspects hyperviscosity, you may have an exam of the back of your eye to check for any changes or bleeding.

Physical exam

It is important to tell your treatment team about any new or worsening symptoms you have that may be related to WM.

Retinal exam

Hyperviscosity can cause small blood vessels inside the eyes to become engorged and have a "sausage link" appearance. A retinal exam can identify this and other changes to the eyes caused by thick blood.

Computed tomography (CT)

CT scans can show if your lymph nodes or organs are enlarged. They are also helpful for determining if cancer has spread beyond the bone marrow.

Peripheral neuropathy

Your brain and spinal cord make up your central nervous system. The human body also has a peripheral nervous system, which includes all the other nerves found throughout the body (peripheral nerves).

Damage to peripheral nerves can cause pain, numbness, tingling, or weakness. This is called peripheral neuropathy. Damage often occurs in the hands and feet but can affect other parts of the body. Peripheral neuropathy is common in people with WM and may be the only source of symptoms.

You may be referred to a neurologist if you have peripheral neuropathy. A neurologist is an expert in nervous system disorders. The neurologist may order testing that includes:

- Nerve conduction studies (NCS)
- Electromyography (EMG)
- Testing for a build-up of an abnormal protein called amyloid in your organs or tissues (amyloidosis). This may include a special stain on the bone marrow sample called Congo red and removal and testing of fat cells (a fat pad biopsy).
- Testing for antibodies against an important protein needed to maintain a healthy nervous system called myelin-associated glycoprotein (MAG). Symptoms of anti-MAG peripheral neuropathy include loss of feeling in fingers and toes, inability to feel vibrations, difficulty walking properly, and shaky hands and legs.
- Testing for antibodies against ganglioside M1, a complex molecule in the nervous system.

Electromyography

An electromyelogram can detect nerve damage in people with symptoms of peripheral neuropathy such as pain, tingling, or numbness.

Do I need treatment?

Simply having an elevated level of IgM in your blood does not mean you need treatment. If you do not have any symptoms, you do not need to be treated. However, if you develop symptoms of the health conditions related to WM that are described in this chapter, treatment is needed. Some common symptoms of these conditions are listed in Guide 1.

Guide 1
WM complications and their symptoms

Hyperviscosity

- Abnormal bleeding
- Vision changes
- Headaches
- Shortness of breath
- Dizziness
- Seizures

Low blood cell counts

- Fatigue
- Frequent infections
- Yellow skin/eyes
- Change in urine color
- Easy bruising/bleeding
- Flu-like symptoms

Neuropathy

Pain, tingling, numbness, swelling, or weakness in different parts of the body

Amyloidosis

- Swelling of legs/ankles or tongue
- Fatigue/weakness
- Shortness of breath
- Skin changes
- Difficulty swallowing
- Weight loss
- Joint pain
- Diarrhea
- Foamy urine

Cryoglobulinemia

- Joint pain
- Purple skin lesions
- Swollen ankles/legs
- Weight loss
- Change in color of feet or hands in cold temperatures

Cold agglutinin disease

- Joint pain
- Fatigue
- Dizziness
- Headaches
- Cold hands and feet
- Dark urine
- Pale or yellow skin
- Muscle weakness

Other

- Enlarged organs (organomegaly)
- Swollen lymph nodes (adenopathy)

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I** trials study the safety and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II** trials study how well the drug or approach works against a specific type of cancer.
- **Phase III** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV** trials study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don’t wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

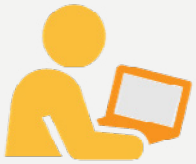
Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo

with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov/

Need help finding a clinical trial?
NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

cancer.gov/contact

Key points

- Bone marrow and blood tests are needed to diagnose WM.
- Testing for a mutated version of the *MYD88* gene is recommended for everyone with suspected WM.
- CT scans of your chest, abdomen, and pelvis are recommended as part of initial testing for WM.
- Other testing may include urine tests and a retinal (eye) exam.
- Peripheral neuropathy is nerve damage that causes pain, numbness, tingling, or weakness.
- Peripheral neuropathy is common in people with WM and may be the only source of symptoms.
- WM only requires treatment if it is causing symptoms.
- Clinical trials give people access to investigational tests and treatments that may, in time, be approved by the FDA.

3
Treatment guide

Waldenström macroglobulinemia (WM) is not curable with current treatments. In people without symptoms, there is no benefit to treatment. WM that is causing symptoms is treated with targeted therapy, chemotherapy, or both. First, you may need to have immunoglobulin M (IgM) removed from your blood using a procedure called plasmapheresis.

In those with symptoms, the goals of treatment are to relieve symptoms and reduce the risk of damage to your organs. Some people will need plasmapheresis before treatment.

Plasmapheresis

Plasmapheresis, also called plasma exchange, is a procedure that removes plasma from the blood. Plasma is the watery, light yellow part of blood that contains IgM and other proteins. Plasmapheresis itself is not a cancer treatment. Rather, it is a way of relieving symptoms and helping your body prepare for systemic therapy.

Who needs plasmapheresis before treatment?

People with symptoms of hyperviscosity should have plasmapheresis right away. After plasmapheresis, systemic therapy should be started as soon as possible.

People without symptoms of hyperviscosity but with a very high level of IgM (4,000 mg/dL or higher) might also have plasmapheresis first if treatment with a targeted therapy called rituximab (Rituxan®) is planned.

Rituximab can cause IgM to increase by 25 percent or more (known as IgM “flare”). This sharp increase in IgM can lead to hyperviscosity, which causes serious side effects. Lowering the level of IgM before treatment with rituximab is important in order to reduce the risk of dangers from hyperviscosity.

What to expect

First, an intravenous line (an “IV”) is put into your vein to remove the plasma. Next, a salt solution and the donated plasma are put back into your blood. Plasmapheresis can take 2 to 3 hours. During this process, you are seated in a reclining chair or asked to lie down on a bed.

The IV is typically put into a vein in your arm. For some people, a catheter may need to be inserted. A catheter is a thin, long tube that is often placed in the chest. This thin tube goes into a large vein and can stay in after the treatment and be used again, if needed.

After plasmapheresis

The level of IgM in your blood will be monitored closely after plasmapheresis. If symptoms of hyperviscosity return, you can have plasmapheresis again. It is not uncommon to need it more than once.

If your IgM level goes above 4,000 mg/dL during treatment with rituximab, you might have plasmapheresis again, even if you do not have symptoms.

You may need a red blood cell transfusion after plasmapheresis. During a transfusion, blood is given to you through an IV. The purpose of a red blood cell transfusion is to replace blood loss that leads to a low red blood cell count (anemia).

Systemic therapy

Systemic therapy is the most effective and widely used treatment for WM. Medicines taken by mouth or put directly into the bloodstream to treat cancer are systemic therapies. The two main types of systemic therapy used to treat WM are targeted therapy and conventional ("cytotoxic") chemotherapy.

Chemotherapy stops the growth of cancer cells, either by killing the cells or stopping them from routinely dividing. Targeted therapy, on the other hand, usually targets specific features on the inside or outside of cancer cells to take advantage of potential weaknesses.

At this time, there are 5 systemic therapy regimens preferred for primary (initial) treatment. See Guide 2. While the regimens in Guide 2 are preferred, other recommended options for systemic therapy are listed in Guide 3.

More information on the following is provided below:

- The types of systemic therapy used to treat WM
- Other care before and during systemic therapy

Guide 2
Preferred systemic therapy regimens

Bendamustine and rituximab (Rituxan®)

Bortezomib (Velcade®), dexamethasone, and rituximab (Rituxan®)

Ibrutinib (Imbruvica®) with or without rituximab (Rituxan®)

Rituximab (Rituxan®), cyclophosphamide, and dexamethasone

Zanubrutinib (Brukinsa®)

Guide 3
Other recommended systemic therapy regimens

Bendamustine

Bortezomib (Velcade®) with or without rituximab (Rituxan®)

Bortezomib (Velcade®) and dexamethasone

Carfilzomib (Kyprolis®), dexamethasone, and rituximab (Rituxan®)

Cladribine with or without rituximab (Rituxan®)

Fludarabine with or without rituximab (Rituxan®)

Fludarabine, cyclophosphamide, and rituximab (Rituxan®)

Ixazomib (Ninlaro®), dexamethasone, and rituximab (Rituxan®)

Rituximab (Rituxan®)

Rituximab (Rituxan®), cyclophosphamide, and prednisone

Rituximab (Rituxan®) and Rituxan Hycela®

Rituximab (Rituxan®) is a targeted therapy widely used to treat WM. It is a type of antibody therapy. For the initial treatment of WM, rituximab is often given in combination with other systemic therapies. If you cannot have rituximab, a similar drug called ofatumumab (Arzerra®) may be given instead.

How it works

Rituximab is an anti-CD20 therapy. Blood cells with cancer (and some healthy blood cells) have a protein on their surface called CD20. Rituxan® targets and attaches to the CD20 protein. This helps your immune system find and attack the cancer cells.

How it's given

The first time you receive rituximab, it will be given by infusion. This means it will be slowly injected into a vein. Your doctor may give you medication beforehand to prevent an allergic reaction. After receiving at least one full infusion, future doses of rituximab can be given as an injection (shot) in the abdomen. This subcutaneous (under the skin) form of rituximab is called Rituxan Hycela®. Patients often prefer this method.

IgM flare

Rituximab can cause the level of IgM in your blood to increase by 25 percent or more. This is called IgM flare. The increase in IgM can cause blood to thicken (hyperviscosity). If blood thickens enough, serious symptoms may develop (symptomatic hyperviscosity). If the level of IgM is high before starting treatment with rituximab, your doctor may recommend having plasmapheresis first. The goal is to help prevent symptomatic hyperviscosity before it starts.

BTK inhibitors

BTK inhibitors are one kind of targeted therapy used to treat WM. They are a type of tyrosine kinase inhibitor (TKI). BTK inhibitors currently used for the treatment of WM include:

- Ibrutinib (Imbruvica®)
- Zanubrutinib (Brukinsa®)
- Acalabrutinib (Calquence®)

How they work

WM starts in lymphocytes called B cells. B cells contain a protein called Bruton's tyrosine kinase (BTK). The BTK protein sends signals that help B cells stay alive and multiply. By blocking these signals, BTK inhibitors help stop cancerous B cells from surviving and multiplying.

Good to know

Up to 4 out of 10 people with WM have a mutation of the *CXCR4* gene. People with a *CXCR4* mutation may have a shorter and slower response to treatment with a BTK inhibitor. If your doctor is considering treatment with a BTK inhibitor, your bone marrow or blood may be tested for *CXCR4* mutations.

How they are given

BTK inhibitors are taken by mouth as a pill. Unlike chemotherapy, which is given in cycles, BTK inhibitors are taken continuously to control WM. Stopping treatment abruptly can cause WM to return and to get worse (progress) quickly. Before you start treatment with a BTK inhibitor, tell your doctor if you are taking any blood thinners.

Side effects

BTK inhibitors can also cause serious side effects, including other cancers, high blood

pressure, bleeding problems, infections, heart rhythm problems, and tumor lysis syndrome (TLS). TLS is a disorder caused by the breakdown products of cancer cells. It can lead to kidney failure and other serious health problems.

Proteasome inhibitors

Proteasome inhibitors are another type of targeted therapy used to treat WM. At this time, there are 3 proteasome inhibitors used for initial treatment of WM:

- Bortezomib (Velcade®)
- Carfilzomib (Kyprolis®)
- Ixazomib (Ninlaro®)

Ixazomib (Ninlaro®) is the only proteasome inhibitor that is taken orally (by mouth) as a capsule. To treat WM, ixazomib is used in combination with dexamethasone and rituximab (Rituxan®).

How they work

All cells contain tiny barrel-shaped machinery called proteasomes. Proteasomes maintain the right balance of proteins in cells by breaking down and destroying unneeded proteins. Proteasome inhibitors prevent proteasomes from getting rid of excess proteins. If proteins in cancer cells continue to build up, the cell will eventually explode and die.

Shingles

Proteasome inhibitors can reactivate the herpes zoster (“shingles”) virus. Shingles is a painful skin rash. It is caused by the same virus that causes chickenpox (varicella zoster). Shingles often forms as a stripe or band of blisters on one side of the body or face. The rash may be more widespread (like chickenpox) in people with weakened immune systems. To reduce the risk of shingles, your doctor may ask you to get the shingles vaccine and take an antiviral medication if systemic therapy that includes Velcade®, Kyprolis®, or Ninlaro® is planned.

Other side effects

Bortezomib (Velcade®) can cause a nerve problem called peripheral neuropathy. Symptoms of this nerve problem include pain, numbness, tingling, swelling, or muscle weakness. It usually affects the hands and feet before other areas of the body. In people who already have neuropathy, bortezomib can make it worse. Your doctor will take this into consideration when recommending a systemic therapy regimen.

Carfilzomib (Kyprolis®) may cause serious damage to the heart and lungs, especially in elderly patients.

Chemotherapy

Most chemotherapy medicines used to treat WM are given intravenously. This means they are slowly put into your bloodstream through a vein. Some are taken by mouth as a pill or injected under the skin, called a subcutaneous injection.

Chemotherapy is often given in cycles of treatment days followed by days of rest. This allows your body to recover before the next cycle. Cycles usually last for several weeks.

Alkylating agents

Bendamustine and cyclophosphamide are chemotherapy medicines used to treat WM and other cancers. They belong to a group of drugs called alkylating agents. Alkylating

agents damage cell DNA to prevent cells from copying themselves.

In damaging DNA, alkylating agents can also damage bone marrow cells. Bone marrow is where new blood cells are made. This stem cell damage can lead to other blood cancers (leukemias) years after treatment.

Nucleoside analogs

Cladribine and fludarabine belong to a group of chemotherapy medicines called nucleoside analogs. Nucleoside analogs are toxic to bone marrow stem cells.

A stem cell transplant may be considered for treating WM that returns more than once after treatment. If there is even a small chance that you may have a stem cell transplant in the future, your doctor will avoid or limit the use of cladribine and fludarabine. Stem cell transplantation is discussed in more detail on page 37.

Stem cell damage could lead to other types of serious blood disorders unrelated to WM, such as leukemia.

BCL-2 inhibitor

BCL-2 is a protein found in high amounts in WM cells. This protein helps prevent cell death. Venetoclax (Venclexta®) is an oral targeted therapy that attaches to and inhibits (blocks) BCL-2, allowing the cancer cells to self-destruct. Venetoclax may be used to treat WM that returns after initial treatment.

Side effects of systemic therapy

Systemic therapy can kill healthy cells in addition to cancer cells. The damage to healthy cells causes potentially harsh side effects. The side effects are different for everyone and depend on the specific medicine(s) given, the dose, and the length of treatment.

Most side effects appear when treatment starts and stop when it is over. However, some side effects may appear years after finishing treatment. Ask your treatment team for a full list of common and rare side effects of each systemic therapy you are receiving.

Common side effects of systemic therapy include:

- Extreme tiredness (fatigue)
- Nausea and vomiting
- Diarrhea
- Constipation
- Loss of taste
- Mouth sores
- Cracked skin
- Hair loss
- Loss of appetite
- Low blood cell counts
- Increased risk of infection
- Bleeding
- Secondary cancers

Other care before and during systemic therapy

IgA and IgG monitoring

Treatment with many of the recommended systemic therapy regimens can cause the levels of two antibodies (IgA and IgG) to become too low. You will have blood tests during treatment to make sure these antibodies are not depleted.

Pneumocystis pneumonia prevention

Pneumocystis pneumonia is a fungal infection of the lungs. It is most often found in people with a weak immune system. Your doctor may prescribe a medication to lower the risk of pneumocystis pneumonia before starting treatment with certain systemic therapy regimens.

Clinical trial

Joining a clinical trial is also an option for treating WM. Participating in a clinical trial allows you to get treatment while also helping cancer researchers learn more about this rare disease. See page 20 for more information on clinical trials.

When treatment is over

After systemic therapy, you will have testing to check treatment results. Testing will likely include a physical exam, blood tests, and computed tomography (CT) scans of your chest, abdomen, and pelvis.

Response to treatment is based on the level of IgM in your blood after systemic therapy. While the IgM level is important, it is not the only factor used to determine if treatment was successful. Some systemic therapy medicines can cause IgM levels to fluctuate, making it difficult to know if the cancer is responding to treatment.

For example, rituximab (Rituxan®) can cause IgM levels to go up for weeks or months (IgM flare). Bortezomib (Velcade®) can cause IgM levels to go down without killing cancer cells, giving a false impression of response to treatment. Other medicines can simply take longer than others to lower IgM levels.

In addition to considering the IgM level, your doctor will consider whether you have any new or worsening symptoms.

Specific criteria are used to determine how well WM responds to treatment. These response categories are also used to guide decision-making about whether more treatment is needed. See Guide 4.

Complete or almost complete response

A **complete response** to treatment means that the IgM level has returned to normal, and no cancer can be detected in your bone marrow using current testing technology.

Guide 4
Response categories for WM

	Description	Next steps
Complete response	• IgM level is in the normal range • No sign of cancer in bone marrow • Any enlarged lymph nodes or organs have returned to normal size • No signs or symptoms of WM	• Watch-and-wait • Monitor IgM
Very good partial response	• A very small amount of IgM remains • Any enlarged lymph nodes or organs have gotten smaller • No new signs or symptoms of WM	
Partial response	• IgM level reduced by more than half • Any enlarged lymph nodes or organs have gotten smaller • No new signs or symptoms of WM	**No symptoms:** • Watch-and-wait • Monitor IgM • Possibly maintenance therapy with rituximab (Rituxan®) **If symptoms:** • Switch to a different systemic therapy regimen
Minor response	• IgM level reduced by less than half • No new signs or symptoms of WM	
No response	• IgM level stayed about the same • The signs and symptoms of WM have stayed about the same	Switch to a different systemic therapy regimen
Progressive disease	• IgM level went up 25 percent or more, or • The signs and symptoms of WM have gotten worse	

A **very good partial response** to treatment means that the IgM level went down by 90 percent or more. Any enlarged lymph nodes or organs have returned to normal size and you have no symptoms.

No further treatment is needed. Your IgM level will be monitored. The IgM level should be measured every 3 months for 2 years, then every 4 to 6 months for an additional 3 years, then every 6 to 12 months thereafter. If the IgM level increases beyond the normal range, it doesn't mean you automatically need more treatment. More treatment is only needed if symptoms return.

Partial or minor response

If the cancer responds to treatment but not completely, whether you need more treatment depends on whether you have symptoms. If you have symptoms, switching to a different systemic therapy regimen is recommended.

If you do not have symptoms, no further treatment is needed. Your IgM level will be monitored. The IgM level should be measured every 3 months for 2 years, then every 4 to 6 months for 3 more years, then every 6 to 12 months thereafter. If the IgM level increases beyond the normal range, it doesn't mean you automatically need more treatment. More treatment is only needed if symptoms return.

If you had a partial or minor response to systemic therapy that contained rituximab (Rituxan®), continuing treatment with rituximab alone as maintenance therapy may be an option. Maintenance therapy may keep you cancer-free for longer.

Stable or progressive disease

If there is no response to treatment, it means the IgM level stayed about the same. This is called stable disease. Progressive disease refers to an increase in IgM level and worsening of WM symptoms. Switching to a different systemic therapy regimen is recommended for either of these response types.

Bone marrow biopsy

Sometimes there can be a disconnect between how well treatment is working and the level of IgM in your blood. If you seem to be responding to treatment and your symptoms are getting better but the IgM level is still high, your doctor may order a bone marrow biopsy to get more information.

While uncommon, it is possible for a slow-growing lymphoma like WM to transform into a fast-growing lymphoma. One reason your doctor may want to do a bone marrow biopsy is to rule out transformation to a fast-growing lymphoma.

A change in your symptoms may be a sign of transformation. Symptoms may include unexplained fever, night sweats, or significant weight loss. These are called "B symptoms." Other symptoms can include enlarged lymph nodes and organs.

If testing finds that WM has transformed, there are NCCN Guidelines for Patients® available addressing other types of lymphomas.

Survivorship

Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the long-term side effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

Your primary care doctor

After finishing cancer treatment, your primary care doctor, also known as a general practitioner (GP) or primary care physician (PCP), will play an important role in your care. Your oncologist (cancer doctor) and PCP should work together to make sure you get the follow-up care you need. Ask your oncologist for a written survivorship care plan that includes:

- A summary of your cancer treatment history
- A description of possible short-term, late, and long-term side effects
- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your PCP
- Clear roles and responsibilities for both your cancer care team and your PCP
- Recommendations on your overall health and well-being

Healthy habits

Monitoring for the return of cancer is important after finishing treatment. But, it is also important to keep up with other aspects of your health. Steps you can take to help prevent other health issues and to improve your quality of life are described next.

Systemic therapies used to treat WM can have serious late or long-term effects, including the development of other (secondary) cancers. Treatment with alkylating chemotherapy drugs in particular can increase the risk of developing other blood cancers. Bendamustine and cyclophosphamide are alkylating agents that may be used to treat WM.

As a cancer survivor, it is especially important to get screened for other types of cancer, such as breast, prostate, colorectal, and skin cancers. Your primary care doctor can tell you which cancer screening tests you should have based on your age and risk level.

Get other recommended health care for your age, such as blood pressure screening, hepatitis C screening, and immunizations (such as the flu shot).

Leading a healthy lifestyle includes maintaining a healthy body weight. Try to exercise at a moderate intensity for at least 150 minutes per week. All patients should have a discussion with their doctor before starting a new exercise regimen. Eat a healthy diet with lots of plant-based foods.

Alcohol may increase the risk of certain cancers. Drink little to no alcohol. If you are a smoker, quit! Counseling and other resources are available. Your treatment team can help.

More information

For more information on cancer survivorship, the following are available at NCCN.org/patientguidelines:

- *Survivorship Care for Healthy Living*
- *Survivorship Care for Cancer-Related Late and Long-Term Effects*

These resources address topics relevant to cancer survivors, including:

- Anxiety, depression, and distress
- Cognitive dysfunction
- Fatigue
- Pain
- Sexual dysfunction
- Sleep disorders
- Healthy lifestyles
- Immunizations
- Employment, insurance, and disability concerns

Relapse

WM may return after treatment. This is called relapse. Relapsed WM is usually treated with systemic therapy, especially if it is the first relapse.

Your doctor will consider the following things when selecting a systemic therapy regimen:

- How soon the cancer returned after treatment
- Whether you can have rituximab (Rituxan®)

You may be treated with the same systemic therapy regimen you had for primary treatment. Or, your doctor may recommend switching to a different regimen. This may be the case if primary treatment was very harsh or caused severe side effects.

The systemic therapy regimens preferred at this time for previously treated WM are listed in Guide 5. Other recommended regimens are listed in Guide 6. These are also good choices for treating relapsed WM.

If the cancer returns more than once, a stem cell transplant may be considered. This potential treatment option is described next.

Guide 5
Preferred systemic therapy regimens for previously treated WM

Bendamustine and rituximab (Rituxan®)

Bortezomib (Velcade®), dexamethasone, and rituximab (Rituxan®)

Ibrutinib (Imbruvica®) with or without rituximab (Rituxan®)

Rituximab (Rituxan®), cyclophosphamide, and dexamethasone

Zanubrutinib (Brukinsa®)

Guide 6
Other recommended systemic therapy regimens for previously treated WM

Acalabrutinib (Calquence®)

Bendamustine

Bortezomib (Velcade®) with or without rituximab (Rituxan®)

Bortezomib (Velcade®) and dexamethasone

Cladribine with or without rituximab (Rituxan®)

Cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (Rituxan®)

Fludarabine with or without rituximab (Rituxan®)

Fludarabine, cyclophosphamide, and rituximab (Rituxan®)

Rituximab (Rituxan®)

Rituximab (Rituxan®), cyclophosphamide, and prednisone

Venetoclax (Venclexta®)

Stem cell transplant

A stem cell transplant may be an option for treating relapsed WM. Blood stem cells are cells that develop into mature blood cells. Stem cells and mature blood cells are made in bone marrow. The goal of a stem cell transplant is to replace unhealthy blood stem cells with healthy ones. This is done by first destroying bone marrow with high doses of chemotherapy, and then transplanting healthy blood stem cells. The healthy blood stem cells form new marrow and blood cells.

The type of stem cell transplant recommended is called high-dose therapy with autologous stem cell rescue (HDT/ASCR). This type of stem cell transplant uses your own healthy stem cells, not stem cells from a donor. The phases of an autologous stem cell transplant are described below.

At this time, an allogeneic stem cell transplant—which uses stem cells from a donor—should only be considered as part of a clinical trial.

Mobilizing stem cells

Blood stem cells are usually taken ("harvested") from blood (as opposed to bone marrow) in an autologous stem cell transplant. However, there aren't many stem cells naturally found in blood. Medicine is used to increase the number of stem cells your body makes, which increases the number of stem cells that enter your bloodstream. This process is called mobilization.

The type of medicine used is called granulocyte-colony stimulating factor (G-CSF), which is given by injection (shots) daily for 5 to 6 days.

Collecting stem cells

If stem cells are being collected from your blood (most common method), a process called apheresis is used. Your blood will be removed from a large vein, most likely in your arm. It will flow through a tube and into a machine that removes stem cells. The rest of your blood will be returned to you in your other arm.

Apheresis typically takes 4 to 6 hours and does not require anesthesia. It may take two or more sessions to obtain enough stem cells. During the procedure, you may have lightheadedness, chills, numbness around the lips, and cramping in the hands.

If the stem cells are being collected from your bone marrow (rarely done for autologous stem cell rescue), a procedure called bone marrow aspiration is used. For this procedure, you will be given either regional anesthesia or general anesthesia. Next, a needle will be inserted through your skin into your hip bone to draw out the bone marrow. The needle must be inserted many times into one or more spots to collect enough marrow. The marrow will then be processed to collect the stem cells.

After apheresis or aspiration, your harvested cells will be combined with a preservative. Then, they will be frozen and stored to keep them alive until the transplant. This process is called cryopreservation.

High-dose chemotherapy

After your stem cells have been harvested, you will receive a high dose of chemotherapy. A high dose of chemotherapy destroys normal cells in the bone marrow. This increases the risk of fatigue due to anemia, the risk of bleeding due to decreased platelets, and the

risk of infection due to the killing of normal white blood cells.

Not every person can tolerate high-dose chemotherapy before the transplant. Your physician will make recommendations about this procedure in consideration of your age and ongoing medical issues.

Transplanting stem cells

When chemotherapy is finished, your harvested stem cells will be put back into your body using a transfusion. A transfusion is a slow injection of blood products through a central line into a large vein. A central line (or central venous catheter) is a thin tube. The tube will be inserted into your skin through one cut, then into your vein through a second cut. Local anesthesia will be used. Placing a central line is usually done by an interventional radiologist.

The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. During engraftment, you will have little or no immune defense. You will need to stay in a very clean environment and may be given an antibiotic to prevent or treat infection. You may also be given a blood transfusion to prevent bleeding and to treat low red blood cell counts (anemia). While waiting for the cells to engraft, you will likely feel tired and weak.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

Key points

- WM is not curable with currently available systemic therapies.
- Targeted therapy, chemotherapy, or both are used to treat WM that is causing symptoms. They are types of systemic therapy.
- Plasmapheresis (plasma exchange) is a procedure that removes plasma from the blood.
- People with symptomatic hyperviscosity should have plasmapheresis right away to relieve symptoms and prevent organ damage.
- People without symptoms of hyperviscosity but with a high IgM level might also have plasmapheresis before starting treatment that includes rituximab.
- Some people will need a red blood cell transfusion after plasmapheresis.
- Joining a clinical trial allows you to get treatment while helping researchers learn more about this rare cancer.
- WM may return after primary treatment. This is called relapse. Relapsed WM is usually treated with systemic therapy.
- An autologous stem cell transplant may be an option for treating WM that returns more than once.
- Managing the long-term effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

4
Making treatment decisions

It is important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer should not be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask your doctor

Possible questions to ask your doctors are listed on this page and the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment. Keep a notebook handy to record answers to your questions.

Questions to ask your doctors about testing

1. What tests will I have for WM?
2. Where and when will the tests take place?
3. How long will they take?
4. What are the risks?
5. How do I prepare for testing?
6. How soon will I know the results and who will explain them to me?
7. Can you tell me about the symptoms of WM?

Questions to ask your doctors about treatment

1. What are my treatment options? Which do you recommend?
2. What will happen if I do nothing? Can I just carefully monitor the cancer?
3. Does this hospital or center offer the best treatment for me?
4. How often will I get treatment, and will I need more than one treatment?
5. How much time do I have to think about my options and/or to get a second opinion?
6. Do my age, general health, and other factors affect my treatment options?
7. How soon should I start treatment? How long does treatment take?
8. Where will I be treated? Will I have to stay in the hospital, or can I go home after each treatment?
9. What can I do to prepare for treatment?
10. What symptoms should I look out for during treatment?
11. How much will treatment cost? How can I find out how much my insurance company will cover?
12. How likely is it that I'll be cancer-free after treatment?

Questions to ask your doctors about side effects

1. What are the side effects of systemic therapy?
2. When can they start?
3. How long will the side effects last?
4. When should I contact the care team about my side effects?
5. What can be done to prevent or relieve the side effects of treatment?
6. Are there any long-term effects of this treatment?

Questions to ask about relapse

1. What are my chances that the cancer will return?
2. What is the treatment for relapsed WM?
3. Will I need a stem cell transplant? Am I healthy enough for a stem cell transplant?

Questions to ask your doctors about clinical trials

1. Is there a clinical trial I can join?
2. What is the purpose of the study?
3. How many people will be in the clinical trial?
4. What are the tests and treatments for this study? And how often will they be?
5. Has the treatment been used before? Has it been used for other types of cancers?
6. What side effects can I expect from the treatment? Can the side effects be controlled?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this treatment doesn't work?
9. How will you know the treatment is working?
10. Who will help me understand the costs of the clinical trial?

What is your experience?

1. Are you board-certified? If yes, in what area?
2. How many patients like me have you treated?
3. Is this treatment a major part of your practice?
4. How many of your patients have had complications?

Resources

American Cancer Society
cancer.org/cancer/waldenstrom-macroglobulinemia.html

CancerCare
cancercare.org/

Cancer.Net
cancer.net/cancer-types/waldenstrom-macroglobulinemia-lymphoplasmacytic-lymphoma/introduction

Cancer Support Community
cancersupportcommunity.org/

International Waldenström's Macroglobulinemia Foundation (IWMF)
iwmf.com/

Lymphoma Coalition
lymphomacoalition.org/

Lymphoma Research Foundation
lymphoma.org/

National Coalition for Cancer Survivorship
canceradvocacy.org/

National Organization for Rare Disorders (NORD)
rarediseases.org/rare-diseases/waldenstroms-macroglobulinemia/

PAN Foundation
panfoundation.org/disease-funds/waldenstrom-macroglobulinemia/

The Leukemia & Lymphoma Society (LLS)
LLS.org/PatientSupport

U.S. National Library of Medicine Clinical Trials Database
clinicaltrials.gov/

MedlinePlus
medlineplus.gov/genetics/condition/waldenstrom-macroglobulinemia/

Take our survey
And help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

Words to know

amyloidosis
A harmful buildup of an abnormal protein called amyloid.

antibody
A protein made by white blood cells that helps fight off infection. Also called an immunoglobulin.

antigen
Any substance that activates the immune system.

autologous stem cell transplant
A treatment that destroys your bone marrow then rebuilds it with your healthy stem cells. Also called high-dose therapy with autologous stem cell rescue (HDT/ASCR).

B cell
One of three types of a white blood cell called a lymphocyte.

beta-2 microglobulin
A small protein found on the surface of many types of cells, and in small amounts in urine and blood.

bone marrow
Soft, sponge-like tissue in the center of most bones where blood cells are made.

bone marrow aspiration
A procedure that removes a liquid bone marrow sample to test for disease.

bone marrow biopsy
Removal of a small amount of solid bone and bone marrow to test for disease.

clinical trial
A type of research that studies how well investigational tests and drugs work in people.

complete blood count (CBC)
A test of the number of blood cells in a sample.

computed tomography (CT)
A test that uses x-rays from many angles to make pictures of areas inside the body.

contrast
A substance put into your body to make clearer pictures during imaging tests.

hyperviscosity
Abnormally thick blood caused by high levels of immunoglobulin M (IgM).

IgM MGUS
A benign condition in which there is a higher-than-normal level of IgM in the blood. Patients with MGUS are at an increased risk of developing WM. Also called monoclonal gammopathy of undetermined significance.

immune system
The body's natural defense against infection and disease.

immunoglobulin
A protein made by white blood cells that helps the body fight off infection. Also called an antibody.

immunoglobulin M (IgM)
The first antibody the body makes to fight a new infection. Found in large amounts in the blood of people with WM.

local anesthesia
A drug-induced loss of feeling in a small area of the body.

lymph
A clear fluid containing infection-fighting white blood cells.

lymphatic system
The tissues and organs that produce, store, and carry white blood cells that fight infection.

lymph node
Small groups of special disease-fighting cells located throughout the body.

lymphocyte
A type of immune cell made in the bone marrow and found in blood and in lymph tissue.

lymphoma
Cancer that begins in white blood cells called lymphocytes that are within the lymphatic system.

lymphoplasmacytic cells
Cells that have features of both lymphocytes and plasma cells.

lymphoplasmacytic lymphoma (LPL)
A type of non-Hodgkin lymphoma that starts in the bone marrow and can cause a shortage of essential blood cells needed by the body. Waldenström macroglobulinemia is the most common form of LPL.

peripheral neuropathy
Nerve damage that causes pain, numbness, tingling, swelling, or weakness in different parts of the body.

plasmapheresis
A procedure that separates and removes plasma from the blood. Also called plasma exchange.

serum immunofixation electrophoresis (SIFE)
A lab test that detects the type of M-proteins in blood.

serum protein electrophoresis (SPEP)
A lab test that measures how many types of antibodies are in blood.

smoldering WM
Asymptomatic Waldenström macroglobulinemia that does not require treatment.

targeted therapy
The use of medicines that can target and attack cancer cells. A type of systemic therapy.

T cell
One of three types of a white blood cell called a lymphocyte.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma, Version 2.2022. It was adapted, reviewed, and published with help from the following people:

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800.789.7366 • pennmedicine.org/cancer

Fred & Pamela Buffett Cancer Center
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402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
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866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
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City of Hope National Medical Center
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Women's Cancer Center |
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Cancer Center
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youhaveus.org
617.726.5130
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