

Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma

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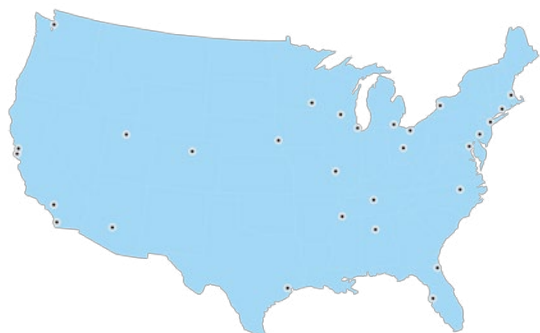
LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you know your options. It explains which cancer tests and treatments are recommended by experts for Waldenström's macroglobulinemia. This cancer is considered to be a type of lymphoma called lymphoplasmacytic lymphoma.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 of the world's leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat Waldenström's macroglobulinemia. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of Waldenström's macroglobulinemia. Key points of the book are summarized in the related [NCCN Quick Guide™](#). NCCN also offers patient resources on chronic lymphocytic leukemia, follicular lymphoma, diffuse large B-cell lymphoma, mantle cell lymphoma, mycosis fungoides, peripheral T-cell lymphoma, and other cancer types. Visit [NCCN.org/patients](https://www.nccn.org/patients) for the full library of patient books as well as other patient and caregiver resources.

About



These patient guides for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from the world's leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.

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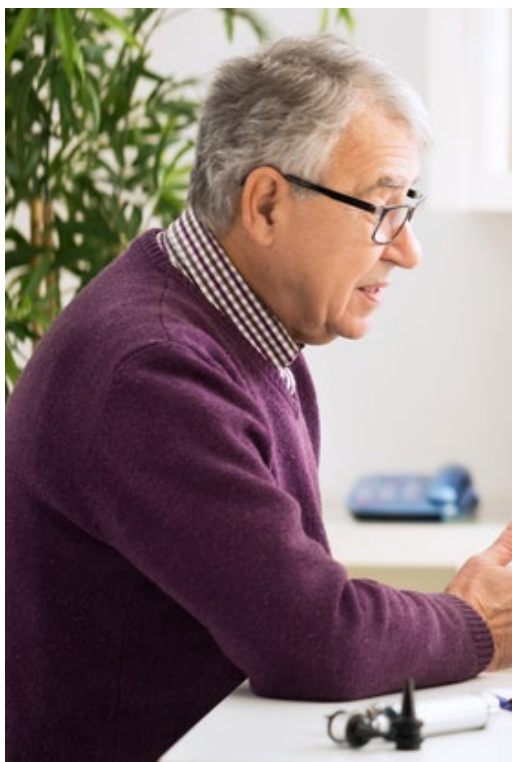
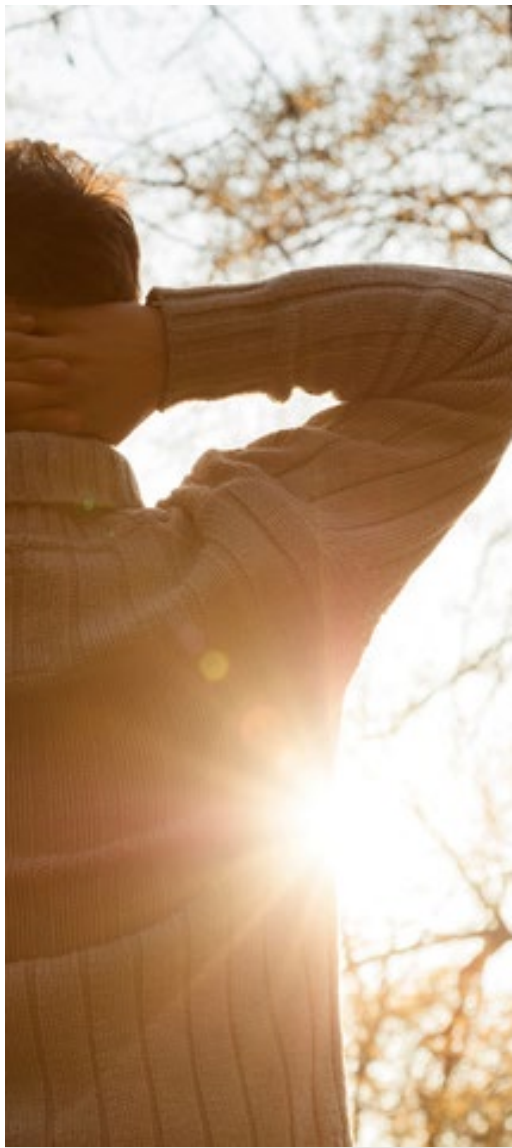
LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients.

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International Waldenstrom's Macroglobulinemia Foundation (IWMF)

The International Waldenstrom's Macroglobulinemia Foundation (IWMF) is dedicated to a simple but compelling vision: *Support everyone affected by Waldenstrom's macroglobulinemia (WM) while advancing the search for a cure.* We endorse the NCCN Patient Guidelines for WM as an excellent source of information for anyone wanting to know more about WM and treatment options.

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Who should read this book?

This book is about **W**aldenström's macroglobulinemia (WM), a type of non-Hodgkin's lymphoma. This type of cancer is considered to be a lymphoplasmacytic lymphoma. This book is for people with WM and those who support them like caregivers, family, and friends.

Where should you start reading?

Starting with Part 1 may be helpful. It explains what WM is and how this cancer is diagnosed. Part 2 lists which health tests and other care are needed before starting treatment. Part 3 briefly describes all the types of treatments so you can understand your options that are listed in Part 4. Tips for making treatment decisions are presented in Part 5.

Does the whole book apply to you?

This book includes information for many situations. Your treatment team can help. They can point out what parts of the book apply to you. They can also give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

The recommendations in this book are based on science and the experience of NCCN experts. However, these recommendations may not be right for you. Your doctors may suggest other tests and treatments based on your health and other factors. If other suggestions are given, feel free to ask your treatment team questions.

Help! What do the words mean?

In this book, many medical words are included. These are words you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don't be discouraged as you read. Keep reading and review the information. Feel free to ask your treatment team to explain a word or phrase that you don't understand.

Words that you may not know are defined in the text or in the *Dictionary*. Acronyms are also defined when first used and in the *Glossary*. Acronyms are short words formed from the first letters of several words. One example is WM for **W**aldenström's macroglobulinemia.

1

Waldenström's macroglobulinemia

8 The lymphatic system

10 Cancer basics

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13 Review



Part 1 talks about Waldenström's macroglobulinemia (WM), which is a type of non-Hodgkin's lymphoma. It is a rare type of lymphoma. Lymphoma is a type of cancer that starts in the cells of the immune system. It can start anywhere in the body. It is helpful to learn about the lymphatic system and what can be done to treat cancer that starts here.

The lymphatic system

The lymphatic system is a part of your immune system. Your immune system defends the body against infection and disease. An infection is caused by germs like bacteria, viruses, or fungi that enter the body and grow out of control. Disease is a medical condition like cancer. Cancer can also grow and spread in your body (metastasize).

The lymphatic system can be found throughout your body. It is made up of lymph, lymph vessels, and lymphatic tissue:

- **Lymph** is clear fluid that contains disease-fighting white blood cells.
- **Lymph vessels** are tube-shaped ducts that carry lymph throughout the body.
- **Lymphatic tissue:**
 - Lymph nodes are groups of small round structures throughout the body.
 - The spleen is an organ that is to the left of the stomach, tucked under the rib cage.

- The thymus is a gland of the immune system that is located behind the top of the breastbone.
- Bone marrow is soft, sponge-like tissue found in the center of most bones, where blood cells are formed.
- Other sites of lymphatic tissue are in the system that breaks down food (digestive system) and in the breathing system (respiratory system).

Lymph

Fluids and plasma leak out of your blood vessels and move around the tissues in your body. Cells release waste and other products into this tissue fluid as well. When tissue fluid increases, it drains into vessels. Some of the tissue fluid drains back into blood vessels. The rest of it drains into lymph vessels.

The fluid inside the lymph vessels is called lymph. The lymph fluid contains white blood cells that fight disease. It also contains plasma, which is the yellowish liquid part of blood that carries blood cells. Lymph travels in lymph vessels, through the lymph nodes to the neck area, to the heart, and back to the bloodstream.

As lymph travels, it is filtered by your lymph nodes. Lymph nodes are a small group of disease-fighting cells. These disease fighting cells make up masses of lymphoid tissue, which form lymph nodes. Lymph nodes are near the lymph vessels throughout your body. The lymph nodes can be found in the middle of your chest, neck, armpit, groin, pelvis, and along your gut.

Lymphocytes

Lymph cells are called lymphocytes. Two main lymphocytes are:

- **B-cells** are a type of white blood cell made in the bone marrow. Most B cells turn into a plasma cell in response to germs. Antibodies, also called immunoglobulins, are proteins made by plasma cells (a type of white blood cell) that helps the body fight infections.
- **T-cells** are a type of white blood cell made in the bone marrow that moves to the thymus. T-cells attacks germs, help the B-cell response, and make cytokines. Cytokines are substances made in the body that boost or activate the body's disease-fighting ability. Cytokines can also be made in a lab.

Lymphocytes are made in bone marrow and then moved by blood to the lymphatic system. Other parts of your body that have many lymphocytes are included in the lymphatic system. In children, the thymus stores T-cells until they are able to fight germs. Germs in blood are filtered and destroyed by lymphocytes within your spleen. Your tonsils kill germs in lymph that enter through your mouth and nose. There are also small clumps of lymphatic tissue in your thyroid, breasts, lungs, liver, eyes, skin, and gut.

Figure 1 Lymphatic system

The lymphatic system kills germs in the body and collects and transports lymph to the bloodstream.

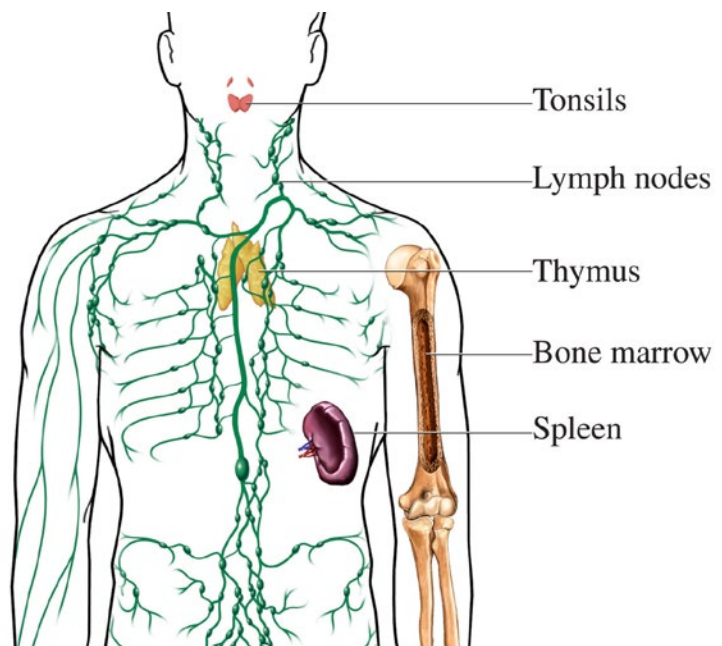


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Cancer basics

Cancer is a disease that starts in the cells of your body. Cells are the building blocks of tissue in the body. The human body contains trillions of cells that serve as these building blocks. Our DNA (deoxyribonucleic acid) controls the cells using instructions on what to do. The instructions are found in the DNA—the genetic code that tells cells what to become (for example, lymph node, thymus, and spleen) and what to do (make hormones, absorb nutrients, and kill germs).

Normal cells grow and divide and repeat the process over and over again. The normal cells are supposed to die when they become old or damaged. If they don't die and new cells start to form, this growth can get out of control. Then an abnormal growth can form that is called a tumor.

Solid tumors can grow anywhere in the body. Other cells can grow out of control in places like the bone marrow and blood. These cells can interrupt how the blood cells form but may not form a tumor.

The blood cancers

Cancer is a disease of abnormal cells that can grow out of control in your body. Cancer can start anywhere in your body, like in organs (for example, breast, lung, stomach) or your blood. Blood cancers (hematologic cancers) can start in the bone marrow or blood cells. Bone marrow is the soft, sponge-like tissue in the center of most bones where blood cells are made. The blood cells are red blood cells (carry oxygen), white blood cells (fight infection), or platelets (form blood clots to control bleeding).

Figure 2 Normal versus cancer cell growth

Normal cells typically stay where they are in the body. But cancer cells can escape from where they started and move to other parts of the body—a process called metastasis. Cancer cells can travel to distant parts of the body through the blood or lymphatic system. When cancer cells settle into new places in the body they can replace or damage healthy cells.

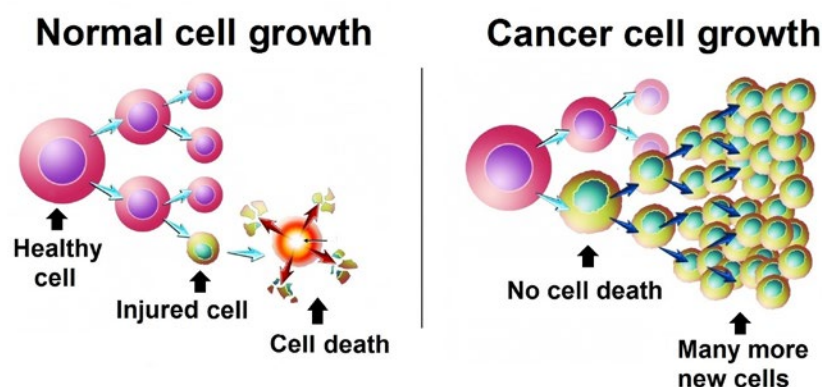


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Cancer can also start in the plasma cells, which is a type of white blood cell. Examples of common blood cancers are multiple myeloma, leukemia, and lymphoma.

Multiple myeloma starts in the plasma cells that make antibodies. Leukemia starts in the white blood cells in the bone marrow or blood. Lymphomas are cancers that start in lymphocytes. Lymphocytes are a type of white blood cell. Lymphomas can be slow growing (indolent) or grow and spread quickly (aggressive).

There are two main types of lymphomas:

- **Hodgkin lymphoma** is defined by finding a type of cell called the Reed-Sternberg cell.
- **Non-Hodgkin's lymphoma (NHL)** includes many other types of cancers that start in the lymphocytes of the immune system.

Most NHLs—90 out of every 100—are B-cell lymphomas. About 10 out of 100 are T-cell lymphomas. There are many types of B-cells and thus, many B-cell cancers. B-cells differ from one another based on the cell's stage of development. As B-cells “mature” they change in their ability to make antibodies.

Antibodies are Y-shaped proteins that are made in response to the presence of antigens. Antigens are substances that are capable of starting an immune response. Some antigens enter your body from outside. Such antigens include viruses, bacteria, chemicals, and pollen. Some antigens are formed inside your body like those found in tissue cells. Antibodies attach to antigens, which triggers a response from your immune system.

Waldenström's macroglobulinemia (WM)

How this cancer starts

WM is a rare cancer of B-cells. It is type of NHL. WM cells share similarities with both plasma cells (multiple myeloma) and lymphocytes (lymphoma). Therefore, the cells are referred to as lymphoplasmacytic cells. WM cells can invade the bone marrow and take up too much space. This causes problems for the other blood cells your body needs to carry oxygen (red blood cells), fight infection (white blood cells), or form blood clots (platelets) to stop bleeding.

For reasons that are not clear, most Waldenström tumor cells make a type of antibody or immunoglobulin called IgM (immunoglobulin **M**). This antibody is “monoclonal,” in that the tumor cells make identical IgM antibodies. The IgM can then collect in blood or urine. These excess antibodies can be measured as a total number. A tumor-specific part of the IgM can also be measured as a monoclonal protein amount or M spike. For a diagnosis of WM, your doctor will also need to check your bone marrow or another tissue for lymphoplasmacytic cells to confirm WM.

Lymphoplasmacytic lymphoma

Lymphoplasmacytic lymphoma (LPL) is a type of NHL. LPL is also a slow-growing lymphoma. It usually is found in the lymph nodes. Lymphoplasmacytic cells are found at diagnosis, but other types of immunoglobulin other than IgM (such as IgA, IgG, or light chains alone) may be present. If IgM is found, it is usually referred to as WM. WM is considered to be a type of LPL because it involves lymphoplasmacytic cells.

Guide 1. Risk factors for WM

Risk factors
• Age- 50 years old or older
• Gender- being male
• Race and ethnicity- more common in white people, and seen in those of Ashkenazi decent
• Family history- family members have WM or other lymphomas
• History of disease- ◦ MGUS (Monoclonal gammopathy of undetermined significance) is when IgM is found in the blood at above normal levels. The level does not go too high or cause symptoms.
*Other risk factors for WM are not known at this time.

Risk factors

WM is a slow-growing type of B-cell NHL. About 1500-2000 people are diagnosed with WM per year. It is considered to be a rare type of cancer. Certain risk factors can be seen with WM. Anything that increases your chances of WM is called a risk factor. Risk factors can be activities that people do, things in the environment, or traits passed down from parents to children through genes. Genes are coded instructions for your cells. [See Guide 1.](#)

Guide 2. Symptoms of WM

Symptoms
• Hyperviscosity and its effects
• Low number of red blood cells
• Enlarged lymph nodes (adenopathy)
• Enlarged organs (organomegaly)
• Nerve problem that causes pain, tingling, and numbness (neuropathy)
• IgM buildup in organs like the heart or kidney (amyloidosis) causing problems
• IgM buildup in places exposed to the cold (cryoglobulins) ◦ For example, your nose, ears, fingers, or toes turn blue or black and can hurt
• IgM breaks down the red blood cells at low temperatures (cold agglutinin disease) ◦ This is a form of hemolytic anemia (red blood cells break down quickly)

Symptoms

A main characteristic of WM is having IgM in the blood. It can be at high levels and this can cause symptoms. The blood becomes thick from IgM. The IgM is a big molecule and can't leave the bloodstream. This is called hyperviscosity. When the blood is too thick, it can't flow right. Hyperviscosity can happen and cause symptoms like weakness, changes with eye sight, headache, stroke-like symptoms, and unexplained bleeding.

[See Guide 2.](#)

Doctors need to assess your health and learn about your symptoms. Keep in mind, symptoms of WM can happen with other medical conditions. For example, some people with WM also have constitutional symptoms. This includes things like fever, extreme tiredness, weight loss, or the chills. Yet, some people with WM have no symptoms at all.

Your doctor may think you have this cancer when he or she finds abnormal levels on a regular blood test or you have symptoms. These things can be found during a routine visit. Currently, there is no screening test for WM. Screening is when tests are done on a regular basis to detect a disease in someone without symptoms.

It is important to tell the doctor how you are feeling during your visit or call if you have any symptoms. Ask what tests you will have to find out what is causing the symptoms. If WM is suspected, your doctor will check for IgM in your blood. If needed, he or she can order a bone marrow aspiration and bone marrow biopsy to confirm a diagnosis of WM. Find out more about testing for WM in Part 2.

Review

- WM is a type of non-Hodgkin's lymphoma.
- Lymphoma is a type of cancer that starts in the cells of the immune system.
- Cancer is a disease of abnormal cells that can grow out of control in your body.
- A type of protein called IgM (immunoglobulin **M**), which in this case is all of the same type, is found in the blood of people with WM.
- A main characteristic of WM is having IgM in the blood. It can be at high levels and this can cause symptoms.
- The blood becomes thick from IgM (hyperviscosity) and can't travel through small blood vessels.

2

Testing for Waldenström's macroglobulinemia

15 Medical history and physical exam

15 Blood tests

16 Imaging tests

18 Biopsy

20 Test results

21 Review



Part 2 lists tests doctors use to learn if your symptoms or signs are caused by WM or another similar disease.

Medical history and physical exam

Two basic tools of diagnosis are when your doctor takes your medical history and does an exam of your body. Your doctor will ask about your medical history, which should include everything that has ever happened to you, related to your health. Your doctor will ask you about:

- Health events in your life including surgeries, accidents, and past illnesses
- Recent sickness
- Medications you are taking now (It is helpful to keep a list of your meds. Include any supplements and over-the-counter medicine you are taking.)
- Family history of disease such as cancer, heart disease, or diabetes

When the doctor checks your body for signs of disease, it is called a physical exam. Doctors often perform a physical exam along with taking a medical history. Your doctor will check your:

- Eyes, ears, nose, and throat
- Lungs, heart, and belly (abdomen)
- Body by feeling and using pressure to see if organs are of normal size, are soft or hard, or cause pain when touched

Blood tests

Blood tests can be done for many reasons including during a routine visit. The results will give the doctor a picture of what is going on in your body. He or she may learn about an unknown disease in the body that has no symptoms, or check for disease like cancer. Blood tests give your doctors information to plan the next steps for other testing or treatment. Blood tests for WM include:

Complete blood count with differential

One of the most common blood tests is the CBC (complete blood count). The CBC is a measure of the various types of cells found in the blood. This test checks the number of white blood cells (fight infection), red blood cells (carry oxygen), and platelets (form blood clots). These numbers are then compared to the normal range for those cells in a healthy person who is about your age. Your blood counts may be low if WM is present. They can also be low for other health reasons.

Comprehensive metabolic panel

Chemicals in your blood come from your liver, bone, and other organs. A comprehensive metabolic panel often includes tests for up to 14 chemicals. The tests show if the level of chemicals is too low or high. Abnormal levels can be caused by cancer or other health problems. These tests will allow your doctor to assess if the kidneys and liver are functioning well.

Immunoglobulin

If WM or another similar disease is suspected, your blood will be tested for certain levels of immunoglobulins. The immunoglobulin (or antibody) found in WM is IgM. SPEP (serum protein electrophoresis), quantitative immunoglobulins, and immunofixation can be used. Immunofixation helps the proteins in your blood stand out when being tested.

These three techniques check the type of immunoglobulin and amount in your blood. This is done by looking at the sample on a gel. Other immunoglobulins are IgA, IgG, IgD, and IgE. They can also be found with these tests. For example, with LPL other immunoglobulins besides IgM may be seen at diagnosis.

Serum viscosity

Viscosity measures how thick the blood can be. High levels of IgM in the blood will cause the blood to be thick and not flow right. This test can be helpful when WM and hyperviscosity is suspected. Your doctor will check if the thickness of the blood is high; cP (centipoise) is the unit of measurement related to thickness of the blood. People with WM may have symptoms when the level is above 4 cP. If the levels of IgM are too high, you may need immediate treatment to relieve symptoms. Many doctors chose to just follow the IgM level since it takes time to get serum viscosity levels back. Sometimes, this level may not be reliable.

Beta-2 microglobulin

Beta-2 microglobulin is a protein in the blood that can be measured at diagnosis. This protein doesn't cause issues but helps the doctor learn how you will respond to treatment. When it comes to making decisions about treatment, more information from research is needed on beta-2 microglobulin.

Imaging tests

Imaging tests are used to take pictures (images) of the inside of your body. Your doctor will want to check the lymph nodes and other organs in your body. Imaging is done to see if the cancer is in more than one area. Imaging tests may also be done during or after treatment to see how the body is responding.

Guide 3. Imaging tests

Imaging test	What is your doctor checking?
X-ray - low-dose radiation to take one picture at a time.	Your lymph nodes and other organs.
Ultrasound - high-energy sound waves make pictures.	Your lymph nodes and other organs.
MRI (magnetic resonance imaging) scan - radio waves and strong magnets make detailed pictures.	Your brain and spinal cord.
CT (computed tomography) scan - x-rays are done to take pictures from many angles.	- Your chest, abdomen, and pelvis. - You can get dye (contrast material) for this type of scan.
PET (positron emission tomography) scan - a tracer detects disease and takes 3-D pictures.	How your body is working. The tracer lights up in certain areas where cells (can be cancer) are moving quickly.

A CT of the chest, abdomen, and pelvis is the most common imaging test for WM. **See Figure 3.** A PET scan or MRI may only be done in certain situations. For example, if Bing-Neel syndrome is suspected you may have an MRI of the brain and spinal cord. This syndrome is rare and affects the central nervous system. It is caused by WM. [See Guide 3.](#)

You will be asked to do certain things before your imaging test. You may need to stop drinking or eating for several hours before certain tests. For an MRI, you will be asked to remove any metal objects (like jewelry) on your body. Let the doctor know if you have any metal objects implanted in your body (for example, artificial joints, stents, or pacemakers) as this may also interfere with the MRI.

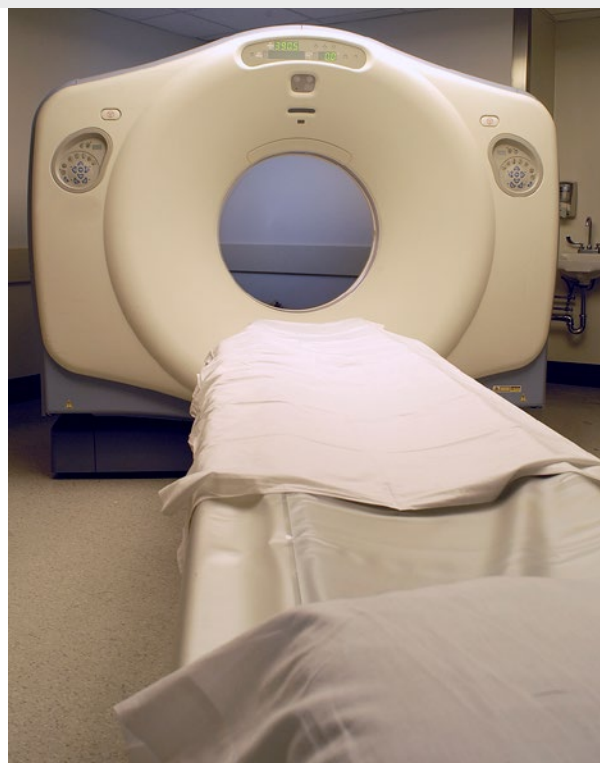
You will be asked to lie down on a table for an ultrasound, MRI, CT, or PET. A PET and CT may be done together. This is called a PET/CT (**positron emission tomography/computed tomography**) scan. This allows your doctors to view the shape and function of organs and tissues.

Tell the doctor if you are allergic to the dye. The dye is called contrast. Let the doctor know if you have any concerns about the machine being used. Ask questions about the test so you can be prepared.

Keep in mind, you will have to wait for the results. The pictures made during imaging tests need to be reviewed by a radiologist. A radiologist is a doctor who's an expert in reading imaging tests. He or she will provide your doctors with a report on what the tests show. It may take several days to get this report.

Figure 3
CT scan machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.



Biopsy

Tissue or fluid must be removed from your body and be tested to diagnose cancer. A biopsy removes the samples of fluid or tissue. Sometimes a sample of tissue from the biopsy does not have enough cells to check for cancer. It can be abnormal but not cancer. If this happens, you will have another biopsy. The most common biopsies for WM are:

- **Bone marrow aspiration** removes a small amount of liquid bone marrow to test for disease.
- **Bone marrow biopsy** removes a small amount of solid bone and bone marrow to test for disease.
- **Lymph node biopsy** removes a small core or an entire lymph node.

Often, these bone marrow tests are done at the same time on the back of hip bone. You may receive a light sedative before the test. You will likely lie on your side as shown in **Figure 4**.

Your doctor will clean your skin then give 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 wider needle will be inserted into the bone and rotated to remove bone and soft marrow. These biopsies may cause bone pain and can bruise your skin for a few days. The samples will be sent to a lab for testing.

Figure 4
Bone marrow biopsy

Doctors use a bone marrow biopsy to remove a sample of bone and marrow for testing.

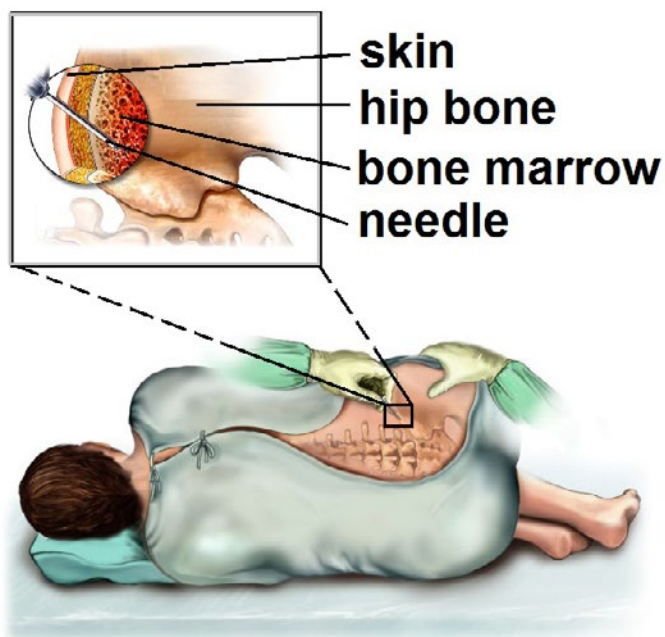


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If needed, a small sample of tissue from a lymph node or organ is removed by incisional biopsy, core biopsy, or FNA (fine-needle aspiration). FNA uses a thin needle with a syringe to take a sample of suspicious tissue. The entire lymph node or abnormal mass of cells (tumor) can be removed during an excisional biopsy to check for cancer. Other lymphomas are usually diagnosed this way.

MYD88 (L265P) test

DNA is a chain of chemicals inside cells that contains coded instructions for making and controlling cells. Your DNA contains instructions from genes that tell your cells how to grow and behave. When bone marrow or other tissue is tested, a lab technician can look at the DNA to see if there is any specific mutation (change) with a diagnosis of WM. This mutation is called MYD88 (L265P). This mutation is common for this cancer. It is found in more than 90 out of 100 people with WM. It may be helpful in determining the diagnosis of WM from other cancers that look like WM. Doctors can also determine if someone will benefit from a getting a cancer drug known as ibrutinib.

CXCR4 test

More than 40 types of CXCR4 mutations can be found in people with WM. CXCR4 mutations are found in 30–40 out of 100 people with WM. It may help doctors understand if and when people will respond to ibrutinib therapy.

Pathology review

The biopsy samples will be sent to a pathologist. A pathologist is a doctor who's an expert in examining cells to find disease. For WM, a hematopathologist may test for cancer. Hematopathologists are pathologists who specialize in testing for disease of the blood and lymph nodes. The hematopathologist will examine the samples using a microscope to see which type of cancer it is. He or she will look at the size, shape, type, and specific features of the cells.

The results of the tests, including those described next, will be recorded in a pathology report. It may take a few days to get a copy. It's a good idea to keep a copy of your pathology report. Your doctors will use the results to plan your treatment.

Protein test

For diagnosis, the hematopathologist needs to study the proteins on the cells' surface. The surface is called the cell membrane. This technique is called immunophenotyping. WM has a common pattern or "signature" of proteins. These proteins the doctor checks for are sIgM+, CD19+, and CD20+. A small number of people with WM express CD5, CD10, and CD23.

Ways to test for these proteins are:

- **Flow cytometry** assesses substances (antigens) on the surface of cells to identify the type of cells present. Blood or bone marrow will be passed through a flow cytometry machine. It uses a dye that reacts to light when checking for the substances.
- **Immunohistochemistry (IHC)** uses a chemical to find specific cell traits involved in abnormal cell growth.

Other tests

Other tests can be done before treatment. This depends on what your doctor decides is necessary. He or she can do certain tests because of treatment they plan to give you.

Your symptoms are also considered before ordering a test. More tests will be done if your hands or feet react poorly to colder temperatures (cryoglobulinemia) or show signs of nerve problems (neuropathy). Symptoms like this will alert your doctor to test for cryoglobulins or do an electromyogram to check what nerves have been affected.

Your doctor may order a coagulation test. This would be done if you have unusual bruising or bleeding. The results of all your tests will help plan your next steps of cancer care.

More tests for WM include:

Cryoglobulin- test for how IgM responds to certain red blood cell antigens at colder temperatures. This can cause red cell breakdown and anemia. This IgM gathers in places that get colder on your body (ears, nose, fingers, or toes) and blocks the blood vessels.

Cold agglutinins- test for cold agglutinins, which are antibodies that destroy red blood cells at colder temperatures. These antibodies can cause the cells to block the blood vessels just like cryoglobulins.

Coagulation- test of the blood to see how well your blood is clotting and how long it takes to clot. Blood clots stop your bleeding. This test can also be done before surgery. For those with a bleeding disorder called VWD (**von Willebrand disease**), testing is only done if bleeding or bruising is present.

Hepatitis B or C (disease of the liver)- test of your blood for this virus. Rituximab can activate hepatitis B. Rituximab is a common drug for WM. People with cryoglobulinemia may have hepatitis C.

Neurology (brain) exam - visit with a specialist to check for nerve damage.

Anti-MAG (myelin-associated glycoprotein) antibody - test for antibodies that can affect your nerves.

Electromyogram - measures the electrical way your muscles work.

Amyloid - test the bone marrow for this abnormal protein. It can build up and cause damage to your nerves (peripheral neuropathy) and organs (amyloidosis).

Retinal exam - exam of the back of your eye to check for any changes or bleeding from hyperviscosity.

Test results

The results from your blood tests, imaging studies, and biopsy will determine whether you get treatment or not. The tests can happen while you are being watched for symptoms or signs of WM. They can continue during treatment and after treatment is over. Blood tests may be done often, where imaging tests will be done at certain time points decided by your doctors. Doctors can use NCCN treatment guidelines to make a care plan. This plan is then based on recommendations from science and the experience of NCCN experts.

Prognostic factors

A prognostic factor is something that affects or helps predict the likely outcome of a disease. A doctor considers your personal traits like age, test results, and extent of cancer when talking about survival (your prognosis).

Treatment factors

Your age, overall health, including other medical conditions, and symptoms play a part in whether or not you get treatment for WM. Your doctor can decide when and which kind you get. This is based on your medical needs and test results. For people with WM, treatment is given to control disease and limit harm to your organs. If you are not having symptoms, you may not be treated right away.

Treatment will not be started for you based on the level of IgM measured in your blood. IgM can go up or down for different reasons. Even the treatment itself can make the level go up or down. As long as you have no symptoms, you may wait to be treated. Your doctor will watch you closely to see if the cancer is growing. This is known as observation. You will both decide when and if you should start treatment.

Staging WM

Staging is the process of rating and describing the extent of cancer in your body. There is no standard staging system (such as Stage I, II, III, etc.) for WM like there is for other cancer types. This is also true for other blood cancers that may not form solid tumors.

Doctors use the International Prognostic Scoring System for WM. This system uses specific factors seen with WM. The factors help group people with WM into high risk, intermediate (middle) risk, and low risk. These factors are considered for prognosis.

The factors include:

- Age- 65 years or older
- Hemoglobin level 11.5 g/dL or less
- Platelet count 100,000/mcL or less
- Beta-2 microglobulin more than 3 mg/L
- IgM level more than 7 g/dL

For people with WM, the high-risk group has more than 2 factors. Intermediate risk is people 65 years or older and those who have two factors. The low-risk group has no factor or those people older than 65 who have 1 factor. The doctor considers the level of risk at diagnosis. More information from research is needed when using the system for treatment decisions.

Review

- Two basic tools of diagnosis are when your doctor takes your medical history and does an exam of your body.
- Blood tests give the doctor information to plan the next steps for other testing or treatment.
- If WM or another similar disease is suspected, your blood will be tested for certain levels of immunoglobulins.
- Tissue or fluid must be removed from your body and tested to diagnose cancer.
- Your age, overall health including other medical conditions, and symptoms play a part in whether you get treatment or not for WM.

What to know about testing...

- ✓ Your doctors will order tests and schedule visits to talk about your care plan. This happens whether you are being watched for symptoms of WM or getting treatment.
- ✓ It is helpful to keep track of your test results at all times. Ask your doctors questions about the results.

3

Overview of cancer treatments

23 Plasmapheresis

23 Chemotherapy

25 Steroids

25 Targeted therapy

28 Immunomodulators

29 Stem cell transplant

30 Clinical trials

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Treatment is given to people with WM who have symptoms. It is helpful to learn about treatment. Ask your doctor what your treatment options are. Part 3 will introduce you to different treatment types for WM. You will also learn how the cancer drugs work in your body.

Plasmapheresis

Plasmapheresis is a process that removes IgM from the blood. It can be given first, before cancer treatment, if you have symptoms of hyperviscosity. Hyperviscosity should be treated as soon as possible to temporarily remove the abnormal IgM in your blood. This can rapidly relieve symptoms. For example, people with peripheral neuropathy that is worsening, or ulcers that are not healing, may need plasmapheresis. Plasmapheresis is sometimes performed once or twice soon after diagnosis. However, it may be recommended that you continue weekly or monthly treatments for a period of time.

Plasmapheresis lowers IgM in your blood so you can feel better. You may have fewer symptoms that can come on suddenly from your chemotherapy drugs. For example, it can be done before you receive treatment with rituximab. The process itself does not stop the cancer from growing. It is more of a treatment to prepare you for cancer-fighting drugs like chemotherapy. You might need an RBC (red blood cell) transfusion after plasmapheresis. Blood is given to you through an IV (intravenous). This transfusion is done to replace blood loss that leads to low RBC count (anemia).

During plasmapheresis

During the process, the plasma is removed from the blood. Plasma is the liquid part of the blood that contains IgM. This plasma needs to be replaced.

An IV is put into a vein to remove the plasma and replace it with donor plasma. A salt solution and plasma from a donor is put back into your blood.

This treatment can be 2 to 3 hours long. During this process, you are seated in a reclining chair or asked to lie down on a table. Most of the time the IV is 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.

Chemotherapy

Chemotherapy, or chemo, is a main systemic cancer treatment. Systemic treatment travels throughout the body to treat or control areas of cancer. Chemotherapy includes drugs that disrupt the life cycle of cancer cells. Some damage DNA directly; others get in the way of processes that help cancer cells build DNA.

Some chemotherapy drugs work when cells are in an active growth phase. During the active growth phase, cells grow and divide to form a new cell. Chemotherapy drugs that disrupt the growth phase work well for cancer cells that are growing and dividing quickly. Other chemotherapy drugs work whether cells are in a growth or resting phase. Chemotherapy can affect both cancer and normal cells.

This kind of treatment can be given in many ways. Most chemotherapy drugs for WM are given as liquids that are slowly injected into a vein by an IV. Some are a pill that is swallowed. Either way, chemotherapy is given in cycles of treatment days usually followed by days of rest. This allows your body to recover before the next cycle.

Cycles usually last for several weeks. Chemotherapy may consist of one or more drugs. When only one drug is used, it is called a single agent. However, not all drugs work the same way, so often more than one drug is used. A combination regimen is the use of two or more chemotherapy drugs together.

Types of chemotherapy

Alkylating agents and antimetabolites are types of chemotherapy used to treat WM. Alkylating agents cause damage to the genetic material in cells. Antimetabolites disrupt a chemical that helps the cell divide.

A steroid, targeted therapy, or both are often added to chemotherapy. These treatments are described later in this chapter. Treatments that combine chemotherapy with drugs, like rituximab, that affect your immune system are called chemoimmunotherapy. Rituximab is a targeted therapy.

Other chemotherapy drugs that are given as the first (primary) therapy or after the first therapy may be toxic to stem cells. These drugs include:

- Alkylating agents such as bendamustine, chlorambucil, and cyclophosphamide.
 - Bendamustine can be given alone or with rituximab.
 - Chlorambucil is given alone.
 - Cyclophosphamide is given with other chemotherapy agents. [See Guide 6 and Guide 7.](#)
- Antimetabolites such as cladribine and fludarabine.
 - Cladribine can be given alone or with rituximab.

- Fludarabine can be alone or with rituximab, or with cyclophosphamide and rituximab.

When treating WM, the effect of the drug on your body is considered, especially if your doctors are considering a stem cell transplant as a future treatment. A stem cell transplant could be a treatment option for certain people with WM. See page 29 for more information.

Part 4 is a guide that explains which treatment options are available for WM. You will learn which regimens may be part of your treatment plan. You will learn more about stem cell transplants later in this chapter.

Side effects of chemotherapy

A side effect can happen when the cancer treatment harms the healthy tissue in your body. Chemotherapy drugs attack fast-dividing cancer cells and can also damage normal cells that are dividing rapidly. The reactions to chemotherapy can differ for people with cancer. Side effects of chemotherapy depend on the chemotherapy drug given, how much, and how long you are given the drug. Your health history is also considered.

Some people have many side effects, while others have few or even none at all. Some side effects can be very serious while others can be hard to cope with, but not serious. Most side effects appear when treatment starts and stop when it is over. However, other side effects are long-term or may appear years later.

Common side effects of chemotherapy are:

- Extreme tiredness (fatigue)
- Nausea and vomiting
- Diarrhea
- Constipation
- Loss of taste
- Mouth sores
- Hair loss
- Not wanting to eat
- Low blood cell counts

Not all side effects of chemotherapy are listed here. Side effects are usually grouped by whether they are more or less likely to occur. Some side effects can be long-term or appear years later like another cancer, heart disease, or not being able to have children (infertility). It is helpful to ask your doctor for a complete list of side effects. Learn how you can prevent and cope with possible side effects of chemotherapy.

Steroids

Steroids are a type of drug that is often used to relieve inflammation. Steroids are toxic to lymphoma cells and therefore have strong anti-cancer effects. Prednisone and dexamethasone are two of these drugs. [See Guide 4](#). Steroid is the short name for corticosteroids.

Steroids are a part of some chemotherapy regimens. They are given on the same days as chemotherapy but only for a few days or a week. Most are pills, but dexamethasone can also be injected. Side effects can happen with steroids. However, most side effects go away once the steroid is stopped.

Common side effects of steroids are:

- Feeling hungry
- Trouble sleeping
- Mood changes
- Slow wound healing
- Upset stomach
- Swelling in the ankles, feet, and hands
- Increased blood sugar
- Increased risk of infection

Targeted therapy

Targeted therapies are drugs that sometimes can directly kill cancer cells. They may also affect the chemical signals between different cells and stop their growth. This treatment is less likely to harm normal cells than chemotherapy. Targeted therapies can be given alone or combined with other drugs. These other drugs are chemotherapy or steroids to treat WM. Common side effects are listed below. Your doctor will have a complete list of side effects. He or she will have information to share with you about the types of targeted therapies and their possible effects on your body.

Below are a few common targeted therapies for WM. Your doctor will offer treatment options based on your health and disease status. This includes your current symptoms, IgM level, and extent of cancer in your body.

Rituximab

Rituximab is a monoclonal antibody that attaches to an antigen called CD20. It is normally found on B cells. **See Figure 5.** The attachment tells the cell to die. Cell death is called apoptosis. Monoclonal antibodies are man-made antibodies that mark cells for destruction by your immune system. Rituximab can be given alone, with chemotherapy, or another cancer drug to treat WM. These drugs include cyclophosphamide, bendamustine, bortezomib, carfilzomib, fludarabine, or cladribine.

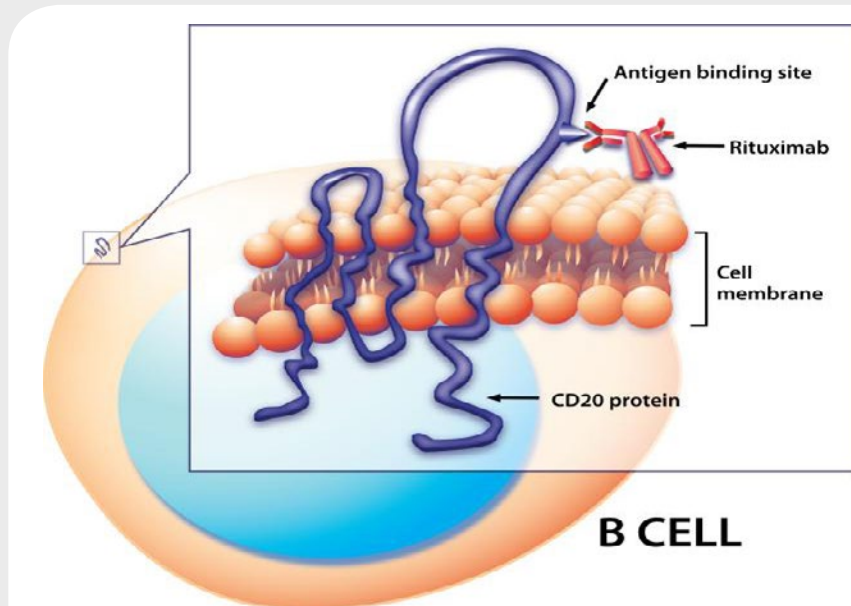
Rituximab is a liquid that is slowly injected into a vein. It can take hours to receive the full dose. Your doctor may give you medication beforehand to prevent an allergic reaction. He or she will decide on the dose (amount given), how long it is given, and how often you get this drug.

Common side effects of rituximab are:

- Extreme tiredness (fatigue)
- Chills
- Infection
- Body aches
- Low blood cell counts

Figure 5
Rituximab attaches to CD20

Rituximab attaches to the CD20 protein on a B-cell.



Derivative work of Rituximab Binding to CD20 on a B Cell Surface by NIAID available at [commons.wikimedia.org/wiki/File:Rituxima_Binding_to_CD20_on_a_B_Cell_Surface_\(6830897205\).jpg](https://commons.wikimedia.org/wiki/File:Rituxima_Binding_to_CD20_on_a_B_Cell_Surface_(6830897205).jpg) under a Creative Commons Attribution 2.0 Generic license.

This drug can cause an IgM flare. The level of IgM goes up due to large amounts being released from dying cells. This flare will cause hyperviscosity and the symptoms that come with it. Your doctor may recommend plasmapheresis before you receive this drug. This depends on whether your IgM level is very high or a test for serum viscosity shows your blood is very thick.

Rituximab also increases your chances for tumor lysis syndrome. This syndrome causes problems in the blood from cells dying and leaving waste. Other problems include heart issues or a blockage and holes in your gut. Serious infections, such as progressive multifocal leukoencephalopathy, are very rare.

If you who can't take rituximab, your doctor can offer ofatumumab. This drug also targets the CD20 antigen. It can briefly increase IgM in the blood. Your doctor will continue to check your IgM level if you receive targeted therapy.

Bortezomib

Bortezomib is another targeted therapy used to treat WM. It is very active in the treatment of WM. It works by a number of mechanisms, one of which stops the proteasome in the cell. The proteasome is the machinery needed to dispose of unwanted proteins in the cell. Bortezomib stops the cell division and causes cell death. It can be given alone, with rituximab, or with rituximab and dexamethasone.

Bortezomib is a liquid that is slowly injected into a vein for a certain period of time. It can also be given as an injection under the skin (subcutaneous). The doctor will decide on the amount given, how long it is given, and how often you get this drug.

Common side effects of bortezomib are:

- Extreme tiredness (fatigue)
- Fever
- Not wanting to eat
- Nausea and vomiting
- Diarrhea
- Constipation
- Low blood cell counts
- Nerve damage (neuropathy)

This drug can cause a certain type of neuropathy called peripheral neuropathy. This type of neuropathy affects the hands and feet. It can begin with sensitivity to cold, pain, burning, and numbness. If someone already has this neuropathy, this drug can make it worse.

Bortezomib can also reactivate the herpes zoster virus. This virus can cause painful blisters or a rash on the skin. Your doctor can give medication to prevent the virus from reactivating.

Ibrutinib

Ibrutinib interferes with the BTK (**B**ruton's **ty**rosine **k**inase). BTK is activated by mutated MYD88. People with CXCR4 mutations show lower response rates and delayed responses to ibrutinib. This molecule of the B-cell helps the cell survive by sending signals. This drug stops the signals so the cell can't grow or divide.

Ibrutinib is given alone. It comes in pill form and is taken by mouth. It is usually taken once a day. Your doctor or pharmacist can answer any questions you have about the dose or time you should take this drug.

Immunomodulators

Common side effects of ibrutinib are:

- Extreme tiredness (fatigue)
- Minor bleeding
- Edema (swelling in hands, feet, or lower legs)
- Diarrhea
- Low platelet count

Before you start ibrutinib, tell your doctor if you are taking any blood thinners. Not all of the side effects of ibrutinib are listed here. Ask your treatment team for a complete list of side effects.

Other targeted therapy:

- Carfilzomib works like bortezomib and has similar side effects. It stops the proteasome machinery inside the cell.
- Alemtuzumab is a monoclonal antibody that attaches to an antigen called CD52. This attachment tells your immune system to destroy the cells. Alemtuzumab is associated with both short-term infections, immune complications, and long-term risks of autoimmune decreases in platelet counts.
- Everolimus targets the mTOR (**m**echanistic **t**arget **o**f **r**apamycin) protein in cells. This protein helps the cells divide and grow.

Carfilzomib is given in combination with rituximab and dexamethasone to treat WM. Alemtuzumab and everolimus are given as a single agent for WM. Everolimus is prescribed as a pill. This is different from the other targeted therapies mentioned above, which are given in liquid form. These three targeted therapies are usually given after other treatment was tried.

The immune system is your body's natural defense against infection and disease. Immunomodulators are drugs that modify different parts of your immune system. The exact function of these drugs is not known.

Lenalidomide and thalidomide treat cancer in more than one way. As immunomodulators, they boost the immune system. They also help stop cancer cells from increasing in number.

Immunomodulators also work like a type of targeted therapy called angiogenesis inhibitors. These drugs stop the growth of new blood vessels. This process is called angiogenesis.

Common side effects of immunomodulators are:

- Extreme tiredness (fatigue)
- Constipation
- Itching and red rash of the skin
- Low blood cell counts
- Nerve damage (neuropathy)

Tell your doctor if you have any side effects and if they get worse over time. Ask your treatment team for a complete list of side effects.

Stem cell transplant

Hematopoietic stem cells are cells that develop into mature blood cells. Hematopoietic stem cells and mature blood cells are made in bone marrow. Cancer or its treatment can damage or destroy the cells in bone marrow. A stem cell transplant replaces damaged or destroyed stem cells with healthy stem cells, which form new marrow and blood cells.

There are two types of stem cell transplant:

- Autologous stem cell transplant uses your own healthy stem cells to repair bone marrow after high doses of chemotherapy. This treatment is also called HDT/ASCR (**high-dose therapy with autologous stem cell rescue**).
 - Healthy stem cells will be collected from you when imaging tests show that cancer treatment is working. You will then receive intense chemotherapy and maybe radiation to destroy any remaining cancer cells.
 - This intense treatment will also destroy bone marrow, so your healthy stem cells will be put back into your body to “rescue” your marrow.
 - Autologous stem cell transplant is more commonly used for WM.
- Allogeneic stem cell transplant uses healthy stem cells that come from a donor. HLA (**human leukocyte antigen**) typing is the test used to check if the donor and your tissue type are a good fit.
 - Chemotherapy will be given to destroy cancer cells and suppress your immune system from attacking the donor cells.

- The transplanted stem cells will form new marrow and attack remaining cancer cells. This attack is known as the GVT (**graft-versus-tumor**) effect.
- There is a serious risk of GVHD (**graft-versus-host disease**). GVHD is when the donated cells see the cells in your body as foreign and attack them.

A stem cell transplant is not used as a first treatment for WM. Your doctor might recommend an autologous stem cell transplant if other treatments are not working well.

Collecting stem cells

The first step of an autologous stem cell transplant is to collect, or harvest, the blood stem cells. Blood stem cells are found in the bone marrow and in the bloodstream. If stem cells are collected from blood, a process called apheresis will be done.

1. Medicine is given to increase the number of stem cells in blood.
2. Some 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.
3. The rest of the blood will be returned through another vein.

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.

Bone marrow aspiration is used to remove bone marrow. For this procedure, either regional anesthesia or general anesthesia will be given. Next, a needle will be inserted through the skin into the 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.

Collection of the bone marrow takes about 1 hour. The entire hospital stay will likely be 6 to 8 hours, which includes recovery time. The aspiration will likely cause some pain and soreness for a few days. Anesthesia may cause nausea, headache, and tiredness. You may need a blood transfusion after the procedure.

After apheresis or aspiration, the 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

Before the autologous transplant, you will likely receive high doses of chemotherapy. High doses are given to kill any cancer cells that may remain after prior treatment. Chemotherapy is often received for several days. The transplant will occur 1 or 2 days later to allow the chemotherapy to clear from your body. Otherwise, the chemotherapy could damage the healthy stem cells.

Transplanting stem cells

After chemotherapy, you will receive your healthy stem cells through 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 and into your vein through a second cut. Local anesthesia will be used. This process can take several hours to complete.

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 weeks.

Until then, you will have little or no immune defense. You may need to stay in the hospital. You may be given an antibiotic to prevent or treat infection. You may also be given a blood platelet transfusion to prevent bleeding and blood transfusion to treat low red blood counts (anemia). While waiting for the cells to engraft, you will likely feel tired and weak.

Clinical trials

A clinical trial is a type of research study that people chose to take part in. Clinical trials help learn how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve your cancer care. This guide has many of those tests and treatments that were found to help people with cancer.

Clinical trials go through levels or phases of testing. These phases help move the research along to find out what works best for people with cancer.

- Phase I looks at how much and how to give the treatment.
- Phase II tests for side effects and how it works on the cancer type.
- Phase III compares the new treatment (or new use of treatment) to what is commonly used.
- Phase IV follows late side effects and if the treatment still works after a long period of time.

All clinical trials have a plan and are carefully led by a medical team. Patients in a clinical trial are often alike with their cancer type and general health. You can join a clinical trial when you meet certain terms. These terms are called eligibility criteria.

If you decide to join a trial, you will need to review and sign a paper called an informed consent form. This form describes the clinical trial in detail, including the benefits and risks. Even after you sign consent, you can stop taking part in a clinical trial at any time.

Some benefits:

- You'll have access to the most current cancer care.
- You will be closely watched by your treatment team.
- You may help other patients with cancer.

Some risks:

- Like any test or treatment, there may be side effects.
- New tests or treatments may not work.
- You may have to visit the hospital more.

Ask your doctor or nurse if a clinical trial may be an option for you. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 5, *Resources*.

Complementary and alternative medicine

CAM (complementary and alternative medicine) is a group of treatments sometimes used by people with cancer. Many CAMs are being studied to see if they are truly helpful.

- Complementary medicines are meant to be used alongside standard therapies, most often for relaxation, improving your health, or to prevent or reduce side effects.
- Alternative medicine is treatment or techniques that are used instead of standard treatments such as chemotherapy or radiation. Some are sold as cures even though they haven't been proven to work in clinical trials.

Many cancer centers or local hospitals have complementary therapy programs that offer acupuncture, yoga, and other types of therapy.

It's important to tell your treatment team if you are using any complementary medicine, especially supplements, vitamins, or herbs. Some of these things can interfere with your cancer treatment. For more information about CAM, ask your doctor and visit the websites in Part 5, *Resources*.

Review

- Plasmapheresis is a process that removes IgM from the blood.
 - Chemotherapy, or chemo, is a main systemic cancer treatment.
 - Steroids are a type of drug that is often used to relieve inflammation.
 - Targeted therapies are drugs that can sometimes directly kill cancer cells.
 - Immunomodulators are drugs that modify different parts of the immune system.
 - A stem cell transplant replaces damaged or destroyed stem cells with healthy stem cells, which form new marrow and blood cells.
 - Clinical trials help learn how to prevent, diagnose, and treat a disease like cancer.

4

Treatment guide

34 Primary treatment

38 Treatment for refractory or relapsed WM

39 Review



Part 4 describes treatment options for people with WM. Patients with WM who have symptoms receive treatment. Options for primary treatment are listed in Guide 4. Guide 5 describes the response to primary treatment. Guide 6 lists next steps based on the response. Guide 7 lists further treatment for WM.

This information is taken from the treatment guidelines written by NCCN experts of WM. These treatment guidelines list options for people with WM in general. Thus, your doctors may suggest other treatment for you based on your health and personal needs. Discuss and decide on your treatment plan with your doctor.

Primary treatment

Your doctor may begin with plasmapheresis. You can get this treatment before systemic therapy is given. Plasmapheresis is done to reduce IgM in the blood that causes hyperviscosity and its symptoms. This type of treatment can prepare your body for the next treatment in line. These options include drugs that are non-stem cell toxic treatment. These drugs will not limit your options for future treatment such as a stem cell transplant.

A stem cell transplant may be an option for a small number of people with WM, especially people with complications of amyloid or who have had multiple relapses. For example, a younger person may have a stem cell transplant in the future. If this is the case, he or she will likely not get certain drugs that can cause damage to normal blood cells, especially if given often. Such damage to cells could possibly lead to other types of serious blood problems, unrelated to WM, such as myelodysplasia and even leukemia.

Guide 4. Primary treatment for WM

Primary treatment
• Drug – non-stem cell toxic treatment ◦ Bortezomib with or without rituximab ◦ Bortezomib / dexamethasone ◦ Bortezomib / dexamethasone / rituximab ◦ Carfilzomab/ rituximab / dexamethasone ◦ Cyclophosphamide / doxorubicin / vincristine / prednisone / rituximab ◦ Ibrutinib ◦ Rituximab ◦ Rituximab / cyclophosphamide / prednisone ◦ Rituximab / cyclophosphamide / dexamethasone ◦ Thalidomide with or without rituximab • Drug – possible stem cell toxic and/or risk of transformation (or unknown) ◦ Bendamustine with or without rituximab ◦ Cladribine with or without rituximab ◦ Chlorambucil ◦ Fludarabine with or without rituximab ◦ Fludarabine / cyclophosphamide / rituximab • Clinical trial

Guide 4 lists the first treatment options for WM. This is called primary treatment. You should get this treatment if you have symptoms of WM. Some of the drugs may work better for you than others. Your doctors have to consider many factors. Thus, your current health, age, and other health problems will affect which treatment you receive. If you are sensitive to any of the drugs, your doctor will start with a safer treatment for your body. As always, a clinical trial is a treatment option.

When your treatment is finished, testing will be done to check treatment results. Imaging tests are used. For example, a CT of the chest, abdomen, and pelvis is useful for checking results. Blood samples are drawn for testing. Your doctor will test your IgM level. However, treatment is not based on the IgM level alone. The level can go up or down with certain drugs. Your doctor will also check if you show any symptoms or signs of WM. If he or she needs more information, a biopsy can be done to confirm cancer.

Guide 5. Primary treatment response

Primary treatment		Response to any primary treatment
Plasmapheresis and Single agent (one drug) or Combination therapy (multiple drugs) or Clinical trial		• Complete response ◦ Normal level of IgM in your body ◦ If disease seen before on imaging- no enlarged lymph nodes or organs ◦ No symptoms or signs of WM
		• Very good partial response ◦ A very small amount of IgM remains ◦ If disease seen before on imaging- decrease in enlarged lymph nodes or organs ◦ No new symptoms or signs of WM
		• Partial response ◦ At least half or a little more than half of IgM remains ◦ If disease seen before on imaging- decrease in enlarged lymph nodes or organs ◦ No new symptoms or signs of WM
		• Minor response ◦ Most of IgM is still in the blood ◦ No new symptoms or signs of WM
		• No response (stable)/disease progression ◦ Stable- disease is stable with continuing symptoms and signs of WM ◦ Progression- disease, signs, and symptoms of WM are getting worse

Guide 5 lists possible responses to any primary treatment. The responses range from complete response, which is no disease found, to disease progression. For a complete response, you will need to have a repeat test to check the IgM again. This will confirm the treatment worked.

You can have other responses to treatment that are very good partial, partial, or minor. If there is no

response to treatment, this means the IgM mostly stayed the same. It is called stable disease. If your disease gets worse (progresses), your doctor will start treatment. When the cancer progresses, you can have signs like anemia, low platelet counts, or enlarged lymph nodes and organs. You can also have symptoms like a fever of 101.1° or higher, night sweats, weight loss, or the other symptoms of WM ([see Guide 2](#)).

Guide 6. Primary treatment response and next steps

Response		Next steps		If disease returns in:
Complete response		• Wait and watch for disease to progress		• Less than 2 years, start a different treatment
		• Consider rituxumab		• Two or more years, try prior treatment or start a new one
Very good partial response		• Wait and watch for disease to progress (no symptoms)		• Less than 2 years, start a different treatment
or		• Consider rituximab (no symptoms)		• Two or more years, try prior treatment or start a new one
Partial response		• Start a different treatment (if symptoms keep going)		• Start a different treatment
or				
Minor response				
No response (stable)/ disease progression		• Start a different treatment		

When deciding if you need more treatment, your doctor will consider your IgM level. He or she will ask if you have new symptoms, they continue, or get worse. If you had enlarged lymph nodes or organs when you were first diagnosed, they will be checked by physical exam or a CT scan. Sometimes lymph nodes near the surface of your skin can be felt. Your next steps will depend on how the first treatment worked in your body.

Guide 6 lists your next steps based on your disease response. Once you have your response, your doctor and you will decide on whether you get more treatment or not. Next steps may be to wait and watch for disease to progress, try a drug treatment, or join a clinical trial. If you are getting a drug treatment, your doctor will consider what you had the first time. If you have no response to treatment and symptoms continue, you will get a different treatment. If the disease comes back, you might be able to try the first drug again or try a new drug. It is important to understand that most people with WM do not enter a complete remission but can still have a very good outcome.

Treatment for relapsed or refractory WM

Guide 7. Further treatment for WM

Relapsed or refractory treatment
• Drug – non-stem cell toxic treatment ◦ Alemtuzumab ◦ Bortezomib with or without rituximab ◦ Bortezomib / dexamethasone ◦ Bortezomib / dexamethasone / rituximab ◦ Cyclophosphamide / doxorubicin / vincristine / prednisone / rituximab ◦ Everolimus ◦ Ibrutinib ◦ Ofatumumab (given alone or with other drugs to people who can't tolerate rituximab) ◦ Rituximab ◦ Rituximab / cyclophosphamide / prednisone ◦ Rituximab / cyclophosphamide / dexamethasone ◦ Thalidomide with or without rituximab • Drug – possible stem cell toxic and/or risk of transformation (or unknown) ◦ Bendamustine with or without rituximab ◦ Cladribine with or without rituximab ◦ Chlorambucil ◦ Fludarabine with or without rituximab ◦ Fludarabine / cyclophosphamide / rituximab • Stem cell transplant ◦ High-dose therapy with stem cell rescue ◦ Allogeneic stem cell transplant (in a clinical trial) • Clinical trial

Guide 7 lists treatment options for WM that didn't respond to (refractory) or reappears (relapsed) after the first treatment. If the disease comes back in less than 2 years, you will try another treatment. If it is

2 years or more, you can get the same treatment you had the first time or try a different drug. This might be a new type of drug used alone or in combination with other drugs.

If a stem cell transplant is an option for you, you will get those drugs that are non-stem cell toxic. Any primary treatment listed in [Guide 7](#) is an option for people who have already been treated for WM. You can also consider a clinical trial.

Next steps

The treatment, drugs, or combination of drugs listed in [Guides 4 and 7](#) are not in any specific order. They are options for your doctors to use when considering your next steps. Your doctor will base your next treatment, whether it is the 2nd, 3rd, or 4th drug, on many factors. The decision will be based on things specific to you. He or she will also consider how you handled the other treatment and how the cancer is responding.

Your next steps will also depend on whether the cancer is gone, stable, or growing. You can still get treatment when the cancer is stable. You can get it when you have no symptoms but had a very good partial, partial, or minor response to treatment. For example, it is recommended that rituximab be given for maintenance. This is called maintenance treatment. The goal of this treatment is to keep things under control.

Follow-up care

Follow-up care is needed after any cancer treatment is finished. Follow-up care includes a medical history, physical exam, lab tests, and imaging tests. During this time, you will have more than one doctor's visit to monitor your health. If the cancer re-appears, a biopsy can be done to confirm there's cancer. If cancer is present, your doctor will try the drugs listed in [Guide 7](#) or recommend a clinical trial.

Review

- Discuss and decide on a treatment plan with your doctor.
- Your doctor may begin with plasmapheresis. You can get this treatment before chemotherapy, targeted therapy, or immunotherapy.
- You should get primary treatment if you have symptoms of WM.
- If needed, you can have further treatment after primary treatment.
- When your treatment is finished, testing will be done to check treatment results.
- Follow-up care is needed after any cancer treatment is finished. Follow-up care includes a medical history, physical exam, lab tests, and imaging tests.

5

Making decisions about your care

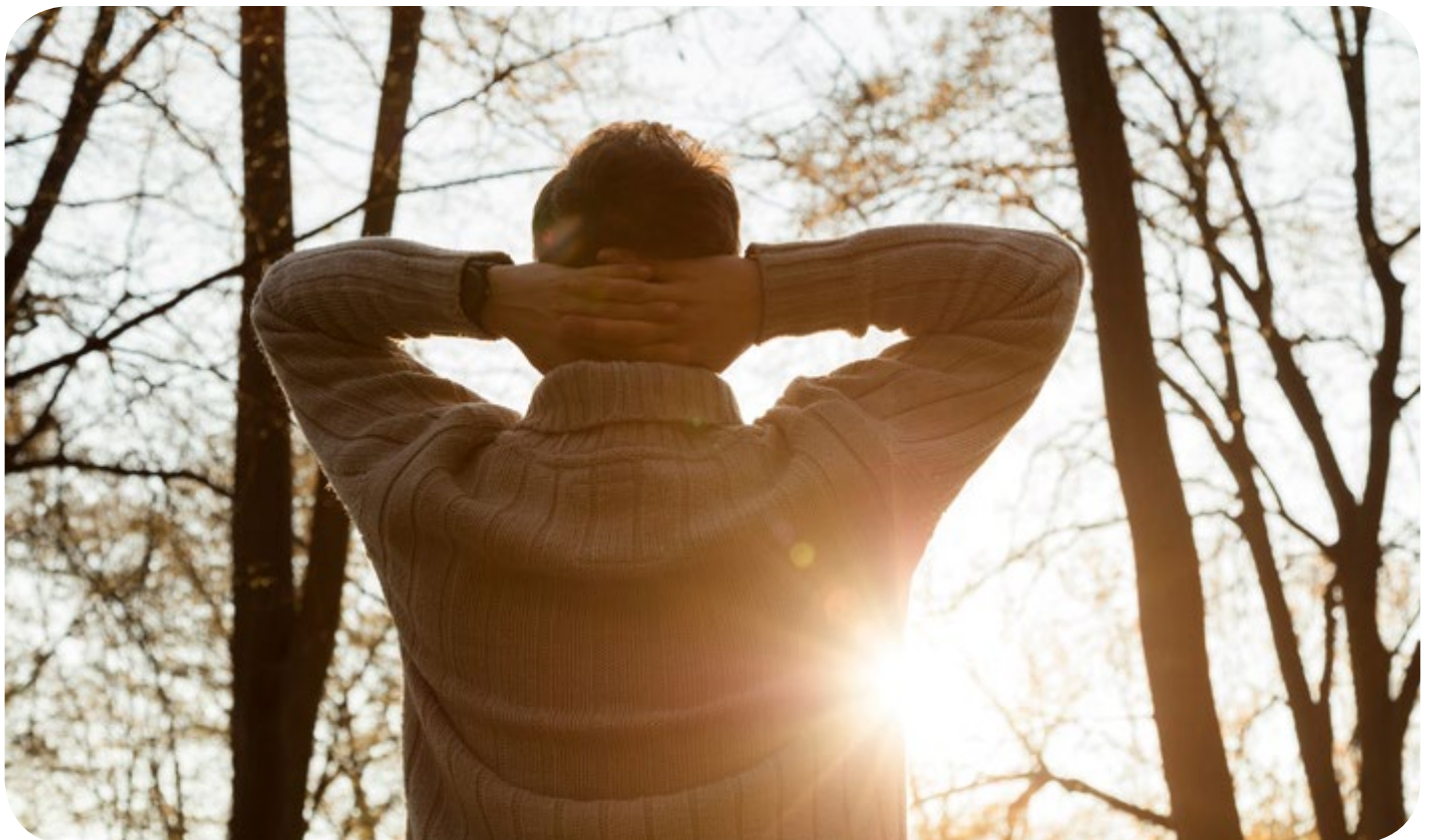
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Learn all you can about WM. This book is a good place to start. Parts 1–4 of this book are meant to help you navigate a diagnosis of WM. Details are given on when to get treatment and what your options may be. Part 5 has sample questions for your doctors and space to create your own questions. In the last section, you will read about getting a 2nd opinion and finding support services.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works best for you when it comes to your health and personal needs.

Questions to ask your doctors

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have a family member or friend with you at these visits. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions on the next few pages are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.

Questions about testing and the results

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. Have any cancer cells spread to other parts of my body?
8. Can you tell me about the symptoms of WM?
9. When will the symptoms start? And if they do, when will treatment start?

Questions about treatment options

1. Will I get treated for WM?
2. What treatment options do I have?
3. Can I join a clinical trial?
4. Does this hospital or center offer the best treatment for me?
5. Can you provide me with the research that supports this treatment plan?
6. How often will I get treatment and will I need more than one?
7. How much time do I have to think about my options?
8. Do I have time to get a 2nd opinion?

Questions about side effects

1. What are the side effects of this treatment?
2. When can they start?
3. How long will the side effects last?
4. When should I call the doctor about my side effects?
5. Are there any medications that can prevent or relieve these side effects?
6. Are there any complementary therapies that might help?
7. Are there any long-term effects of this treatment?

Questions about clinical trials

1. What clinical trial is right for me?
2. How many people will be in the clinical trial?
3. What are the tests and treatments for this study? And how often will they be?
4. How long will I be in the clinical trial?
5. Will I be able to get other treatment if this doesn't work?
6. How will you know the treatment is working?
7. Who will help me understand the costs of the clinical trial?

Learn about your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse, partner, or caregiver may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some other ways to decide on a treatment plan that works best for you are discussed next

Getting a 2nd opinion

Even if you like and trust your doctor, it is helpful to get a 2nd opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- Check with your insurance company about its rules on 2nd opinions. You want to know about out-of-pocket costs for 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 2nd opinion. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.

If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. If you're not sure what to do, get a 3rd or 4th opinion. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with WM. If your hospital or community doesn't have support groups for people with WM, check out the websites on the next page. You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and to those with children, so they can connect and get support.

What to remember...

- ✓ Every treatment option has benefits and risks. Consider these when deciding which option is best for you.
- ✓ Talking to others may help identify benefits and risks you haven't thought of.

Websites

American Cancer Society

What is Waldenström macroglobulinemia?

<http://www.cancer.org/cancer/waldenstrommacroglobulinemia/detailedguide/waldenstrom-macroglobulinemia-w-m>

Clinicaltrials.gov

<https://www.clinicaltrials.gov/>

Leukemia and Lymphoma Society

Waldenström Macroglobulinemia Facts (PDF)

http://www.lls.org/sites/default/files/file_assets/waldenstrommacroglobulinemia.pdf

National Cancer Institute

Adult Non-Hodgkin Lymphoma

Treatment (PDQ®)—Patient Version

<https://www.cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq>

NCCN Guidelines for Patients®

www.nccn.org/patients

NCCN Find a clinical trial

https://www.nccn.org/patients/resources/clinical_trials/find_trials.aspx

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.

Glossary

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51 Acronyms

Dictionary

allogeneic stem cell transplant

A cancer treatment that destroys bone marrow then replaces it by adding healthy blood stem cells from a donor.

anesthesia

Loss of feeling with or without loss of wakefulness that is caused by drugs.

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 cancer treatment that destroys bone marrow then replaces it by adding healthy blood stem cells from the patient. Also called an HDT/ASCR (high-dose therapy with autologous stem cell rescue).

b symptoms

Fevers, heavy night sweats, and weight loss without dieting caused by B-cell cancers.

B-cell

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

beta-2 microglobulin

A small protein made by many types of cells.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

bone marrow

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

bone marrow aspiration

Removal of a small amount of bone marrow that is liquid to test for disease.

bone marrow biopsy

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

chemotherapy

Drugs that stop the life cycle of cells so they don't increase in number.

chromosome

Stands of genetic material inside of cells.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

complete blood count (CBC)

A test of the number of blood cells in a sample.

comprehensive metabolic panel

Tests of up to 14 chemicals in your blood.

computed tomography (CT)

A test that uses x-rays to view body parts.

contrast

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

deoxyribonucleic acid (DNA)

A chain of chemicals inside cells that contains coded instructions for making and controlling cells.

diagnose

To identify a disease.

differential

Measurement of the different types of white blood cells present in a blood sample.

fatigue

Severe tiredness despite getting enough sleep that limits one's ability to function.

flow cytometry

A test that looks at certain substances on the surface of cells to identify the type of cells present.

gene

Instructions in cells for making and controlling cells.

general anesthesia

A controlled loss of wakefulness from drugs.

human leukocyte antigen (HLA) typing

A blood test that finds a person's unique set of proteins on cells.

imaging test

A test that makes pictures (images) of the inside of the body.

immune system

The body's natural defense against illness.

immunoglobulin

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

immunohistochemistry (IHC)

A test of cancer cells to find specific cell traits involved in abnormal cell growth.

immunomodulator

A type of drug that modifies some parts of the body's disease-fighting system.

liver

Organ that removes waste from the blood and helps to digest food.

local anesthesia

A controlled loss of feeling in a small area of the body caused by drugs.

lymph

A clear fluid containing white blood cells.

lymph node

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

lymph vessel

Tube-shaped ducts that carry lymph throughout the body.

lymphatic system

A network in the body that collects and transports a fluid (lymph) and fights germs.

lymphocyte

A type of white blood cell that helps protect the body from illness.

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.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

metastasis

The spread of cancer cells from the first tumor to another body part.

medical history

All health events and medications taken to date.

monoclonal antibody

Man-made antibodies that attach proteins on cancer cells.

pathologist

A doctor who's an expert in testing cells to find disease.

physical exam

A review of the body by a health expert for signs of disease.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

regional anesthesia

A type of drug used for short-term loss of feeling or awareness in a part of the body without loss of wakefulness.

sedative

A drug that helps a person to relax or go to sleep.

side effect

An unplanned physical or emotional response to treatment.

spleen

An organ to the left of the stomach that helps protect the body from disease.

stem cell transplant

A cancer treatment that destroys bone marrow then replaces it by adding healthy blood stem cells.

steroid

A drug used to reduce redness, swelling, and pain, but also to kill cancer cells.

targeted therapy

Drugs that stop the growth process that is specific to cancer cells.

T-cell

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

thymus

A gland located in the throat, just beneath the voice box.

tonsil

A group of tissue within the throat that contains many white blood cells called lymphocytes and fights germs that enter the mouth and nose.

tumor lysis syndrome

A condition that occurs when many cancer cells die very quickly and release their contents into the blood, which can damage the kidneys and other organs.

Acronyms

BTK

Bruton's tyrosine kinase

CAM

complementary and alternative medicine

CBC

complete blood count

CNS

central nervous system

cP

centipoise

CT

computed tomography

DNA

deoxyribonucleic acid

FNA

fine-needle aspiration

GVHD

graft-versus-host disease

GVT

graft-versus-tumor

HDT/ASCR

high-dose therapy with autologous stem cell rescue

HLA

human leukocyte antigen

IHC

immunohistochemistry

ultrasound

A test that uses sound waves to take pictures of the inside of the body.

x-ray

Use of small amounts of radiation to make pictures of the insides of the body.

IgM

immunoglobulin M

IV

intravenous

LPL

lymphoplasmacytic lymphoma

MAG

myelin-associated glycoprotein

MRI

magnetic resonance imaging

NCCN®

National Comprehensive Cancer Network®

NHL

non-Hodgkin's lymphoma

PET

positron emission tomograph

RBC

red blood cell

SPEP

serum protein electrophoresis

VWM

von Willebrand disease

WM

Waldenström's macroglobulinemia



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Chronic Myelogenous Leukemia
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Hodgkin Lymphoma
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Lung Cancer (Non-Small Cell Lung
Cancer)
Lung Cancer Screening
Malignant Pleural Mesothelioma
Melanoma
Multiple Myeloma
Myelodysplastic Syndromes
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 Follicular Lymphoma
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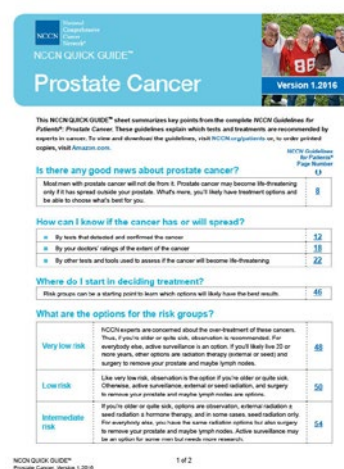


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cancer.northwestern.edu

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mayoclinic.org/departments-centers/mayo-clinic-cancer-center

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800.525.2225
mskcc.org

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066
cancer.osu.edu

Roswell Park Cancer Institute
Buffalo, New York
877.275.7724
roswellpark.org

Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine
St. Louis, Missouri
800.600.3606
siteman.wustl.edu

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mdanderson.org

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