Waldenström Macroglobulinemia

Lymphoplasmacytic Lymphoma

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The International Waldenstrom’s Macroglobulinemia Foundation (IWMF) is dedicated to a simple but compelling vision: A world without WM (Waldenstrom’s macroglobulinemia). Our mission is to Support and educate 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. iwmf.com

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Waldenström basics

What is Waldenström macroglobulinemia?

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 Waldenström macroglobulinemia?

Waldenström macroglobulinemia is a type of lymphoma called 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 a non-Hodgkin lymphoma called 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 the essential blood cells needed by your body 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.

- 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

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 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 in your body will start to cause health issues that you can notice (symptoms).
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.

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.
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 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.

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).

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.
Testing for WM

Bone marrow tests
If your doctor suspects WM, one of the first things he or she will do is test your bone marrow.

Sampling bone marrow
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 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 a small piece of bone and soft marrow. These biopsies may cause bruising and tenderness or pain at the biopsy site.

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

Bone marrow 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 microscope, it is likely that you have WM. Other testing will also be done to confirm the diagnosis.
These tests are explained in greater detail on the following pages.

**Pathology review**
After a biopsy, the removed tissue will be sliced into very thin layers that are placed on a glass slide and examined under a microscope. If you have LPL or WM, there will be abnormal cells that have features of both lymphocytes and plasma cells. These cells are called lymphoplasmacytic cells.

**Protein tests**
The removed bone marrow will also be 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 tests**
Genes (pronounced "jeans") 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, while others 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.

**MYD88 mutation**
Most people with WM have an abnormal (mutated) version of a gene named 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.

Ibrutinib (Imbruvica®) is a targeted therapy used to treat WM. Ibrutinib works better in people with the MYD88 mutation. Your doctor will take this into consideration when recommending a treatment plan.

**CXCR4 mutations**
Up to 4 out of 10 people with WM have a mutation of the CXCR4 gene. People with a CXCR4 mutation may respond less well to treatment with ibrutinib (Imbruvica®). If your doctor is considering treatment with ibrutinib, your bone marrow should be tested for CXCR4 mutations.
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)

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 usually 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.

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

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.

Cryoglobulinemia
Cryoglobulins are one type of cold-sensitive antibody that can be found in people with WM. They may or may not cause symptoms. 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. If your doctor thinks you might have cryoglobulinemia, he or she will order a test called a cryocrit.

Cryoglobulins can interfere with blood IgM level measurements by causing the level of IgM to be lower than it actually is. If the test finds cryoglobulins, it is recommended that you have your blood IgM level tested again, and that all future blood IgM measurements be done under warm conditions.

Cold agglutinin disease
Cold agglutinins are a less common type of cold-sensitive antibody. They may or may not cause symptoms. 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 RBCs 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
The targeted therapy rituximab (Rituxan®) is widely used to treat WM. Rituximab 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 don’t have any signs or symptoms of the disease. Before starting treatment with rituximab, everyone should 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 with rituximab and for several months afterwards. 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.

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 to creatinine ratio
- Electrolytes
- A protein made by the liver called albumin
- Calcium
- Uric acid
- An enzyme called lactate dehydrogenase (LDH)
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 complication 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.

Imaging tests
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 contrast dye is used to make the pictures clearer. The dye will be 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.

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)

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 caused by hyperviscosity.
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.
WM and 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 of 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.

Neurology referral
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 a high level of IgM in your blood does not mean you necessarily need treatment. If you don’t 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
Complications of WM and their symptoms

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<td>Frequent infections</td>
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<td>Adenopathy</td>
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Waldenström basics

Review

- Waldenström macroglobulinemia (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.

- IgM is the largest antibody. It has a bulky, ball-like shape. Large amounts of this bulky antibody can cause blood to become abnormally thick. This is called hyperviscosity.

- Hyperviscosity is a serious side effect of WM. It can cause abnormal bleeding, vision problems, nervous system problems, and cardiovascular (heart and lung) issues.

- Hyperviscosity can also cause dangerous bleeding or clotting problems. They often involve the eyes, gums, and skin.

- Bone marrow and blood tests are needed to diagnose WM.

- Everyone with suspected WM should be tested for a mutated version of the MYD88 gene.

- If you might be treated with a targeted therapy called ibrutinib (Imbruvica®), you should be tested for mutations of the CXCR4 gene.

- WM only requires treatment if it is causing symptoms.
2
Overview of treatments for WM

20 Plasmapheresis
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This chapter describes the types of treatments used for Waldenström macroglobulinemia, as well as a procedure that may be needed before treatment.

Plasmapheresis

Plasmapheresis is a procedure that removes plasma from the blood. Plasma is the liquid part of blood that contains immunoglobulin M (IgM). Plasmapheresis itself is not a cancer treatment. Rather, it is a way of relieving symptoms and helping your body prepare for systemic therapy. Another name for plasmapheresis is plasma exchange.

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. 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.

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

Systemic therapy

A cancer treatment that affects the whole body is called a systemic therapy. Medicines taken by mouth or put directly into the bloodstream to treat cancer are systemic therapies.

Types of systemic therapy include:

- **Chemotherapy**
- **Targeted therapy**
- **Immunotherapy**

Systemic therapy medicines may be used alone, but are often combined to treat cancer. For example, a common systemic therapy regimen used to treat WM includes both a chemotherapy medicine (bendamustine) and a targeted therapy (rituximab).

**Chemotherapy**

Chemotherapy is likely the most well-known systemic therapy. There are many types of chemotherapy medicines that work in different ways to treat cancer.

**How is chemotherapy given?**

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.

**Stem cell-toxic chemotherapies**

Some chemotherapy medicines are toxic to bone marrow stem cells. These medicines
should be avoided if you might have a stem cell transplant as a future treatment. Blood and bone marrow stem cell transplants are discussed in more detail on page 24.

**Side effects of chemotherapy**
Chemotherapy damages both cancer cells and healthy cells. Damage to healthy cells is what causes the potentially harsh side effects of chemotherapy. Common side effects of chemotherapy include:

- Increased risk of infection
- Bleeding
- Secondary cancers

Everyone reacts to chemotherapy differently. The side effects you experience will depend on the 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.

Chemotherapy

Chemotherapy is one of the most widely used types of systemic therapy. It is often used in combination with a targeted therapy called rituximab to treat Waldenström macroglobulinemia.
Targeted therapy
Targeted therapy is a type of systemic therapy that can target and attack specific types of cancer cells. It tends to harm normal cells less than chemotherapy, which means the side effects are usually less harsh.

Rituximab (Rituxan®)
Rituxan® is a targeted therapy widely used to treat WM. While it may be used alone, rituximab is often given in combination with chemotherapy to treat WM.

How it works
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
Rituximab is a liquid that is slowly injected into a vein. 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 will be given, and how often you will get this drug.

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). Some people may need plasmapheresis before starting treatment with rituximab to reduce the risk of symptomatic hyperviscosity.

Pneumocystis jiroveci pneumonia (PJP)
PJP is a fungal infection of the lungs. It is most often found in people with a weak immune system. Symptoms include shortness of breath, fever, night sweats, weight loss, and dry cough. Your doctor may prescribe a medication to lower the risk of pneumocystis pneumonia if systemic therapy with the following regimens is planned:

- Bendamustine and rituximab (Rituxan®)
- Fludarabine (Fludara®), cyclophosphamide, and rituximab (Rituxan®)
Ibrutinib (Imbruvica®)
Ibrutinib is a type of targeted therapy called a tyrosine kinase inhibitor (TKI). Ibrutinib given with or without rituximab is one of four regimens preferred by NCCN experts for the initial treatment of WM.

How it works
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, ibrutinib helps stop cancerous B cells from surviving and multiplying.

Good to know
Ibrutinib works better in people with the MYD88 mutation. Most people with WM have this mutation. However, people with a CXCR4 mutation may respond less well to treatment with ibrutinib. If your doctor is considering treatment with ibrutinib, your bone marrow or blood should be tested for CXCR4 mutations.

How it’s given
Ibrutinib is taken by mouth as a pill. Unlike chemotherapy, which is given in cycles, ibrutinib must be taken continuously to control WM. Stopping ibrutinib abruptly can cause WM to return and to get worse (progress) quickly.

Before you start treatment with ibrutinib, tell your doctor if you are taking any blood thinners.

Proteasome inhibitors
Another type of targeted therapy used to treat Waldenström macroglobulinemia is called a proteasome inhibitor.

At this time, there are three proteasome inhibitors used to treat WM:

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

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.

Side effects
Bortezomib (Velcade®) can cause a nerve problem called peripheral neuropathy. Peripheral neuropathy causes 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. Systemic therapy regimens that include bortezomib should therefore be avoided in people with neuropathy related to WM.
Bortezomib (Velcade®) and carfilzomib (Kyprolis®) 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 called acyclovir if systemic therapy that includes Velcade® or Kyprolis® is planned.

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

**Steroids**

The word steroid is short for "corticosteroid." Some chemotherapy regimens for WM include steroids. Steroids are drugs usually used to relieve inflammation, but some also have anti-cancer effects. Dexamethasone and prednisone are steroids used with chemotherapy to treat WM. Prednisone is taken as a pill; dexamethasone can be injected or swallowed.
Overview of treatments for WM

Stem cell transplant

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.

Stem cell transplant is not used for the initial treatment of WM. It may be an option for treating WM that returns after treatment (relapsed WM). If a stem cell transplant is needed, the type of transplant recommended by NCCN experts is called an autologous stem cell transplant.

Autologous stem cell transplant

Also called high-dose chemotherapy with autologous stem cell rescue (HDT/ASCR), this type of transplant uses your own stem cells.

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.

Until then, you will have little or no immune defense. You will need to stay in a very clean environment. You 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.

**Allogeneic stem cell transplant**

An allogeneic stem cell transplant uses stem cells from a donor. This type of stem cell transplant is not used often in the management of Waldenström macroglobulinemia. NCCN experts recommend that an allogeneic stem cell transplant only be pursued as part of a clinical trial.
Clinical trials

New tests and treatments aren’t offered to the public until they are deemed safe for testing and potentially effective. They first need to be studied in a way that is regulated by the FDA and other governmental agencies.

A clinical trial is a type of research that studies the safety and effectiveness of tests and treatments. They are done at all stages of a disease like WM. When found to be safe and effective, they may become tomorrow’s standard of care.

Joining a clinical trial can have both benefits and risks. You will need to weigh the potential benefits and downsides to decide what is right for you. To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to ensure that any progress is because of the treatment and not because of differences between patients. To join, you’ll need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits.

Ask your treatment team if there is an open clinical trial that you can join. 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 the chapter, Making treatment decisions.

Clinical trials
Because of clinical trials, the tests and treatments in this book are now widely used to help people with Waldenström macroglobulinemia.
Review

- Plasmapheresis is a procedure that removes plasma from the blood. Plasma is the liquid part of blood that contains immunoglobulin M (IgM).

- A cancer treatment that affects the whole body is called a systemic therapy.Chemotherapy and targeted therapy are systemic therapies.

- Rituximab (Rituxan®) is a targeted therapy widely used to treat WM. It is often used in combination with chemotherapy.

- Rituximab can cause the level of IgM in your blood to increase by 25 percent or more. This is called IgM flare.

- Ibrutinib (Imbruvica®) is a type of targeted therapy called a tyrosine kinase inhibitor (TKI). Ibrutinib works better in people with the MYD88 mutation. People with a CXCR4 mutation may respond less well to treatment with ibrutinib.

- Proteasome inhibitors are another type of targeted therapy. Proteasome inhibitors currently used to treat WM include bortezomib (Velcade®), carfilzomib (Kyprolis®), and ixazomib (Ninlaro®).

- Stem cell transplant is not used for the initial treatment of WM. An autologous stem cell transplant may be an option for treating WM that returns after treatment (relapsed WM).

- Clinical trials can help researchers learn how to prevent, diagnose, and treat WM.
3

Treatment guide: WM

- Primary treatment
- When treatment is over
- Previously treated WM
- Review
Waldenström macroglobulinemia (WM) that is causing symptoms is treated with chemotherapy, targeted therapy, or both. Before starting treatment, you may need to have immunoglobulin M (IgM) removed from your blood using a procedure called plasmapheresis.

Primary treatment

Waldenström macroglobulinemia (WM) that is causing symptoms requires treatment. The goals of treatment are to relieve your symptoms and reduce the risk of damage to your organs. Before starting primary treatment, some people will need plasmapheresis.

Plasmapheresis
Plasmapheresis is a procedure that removes plasma from the blood. Plasma is the part of blood that contains IgM. Plasmapheresis itself is not a cancer treatment. Rather, it is used to relieve symptoms and limit organ damage before starting systemic therapy. See page 21 for more information about what to expect during plasmapheresis.

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 before treatment if systemic therapy that includes rituximab (Rituxan®) is planned.

Rituxan® can cause IgM to increase by 25 percent or more ("IgM flare"). This sharp increase in IgM can lead to hyperviscosity, which causes serious side effects. Lowering the level of IgM before treatment is important in order to reduce the risk of hyperviscosity.

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 4000 mg/dL during treatment with Rituxan®, you might have plasmapheresis again, even if you don’t have symptoms. Some people will need a red blood cell transfusion after plasmapheresis.

Systemic therapy
Systemic therapy is the most effective and widely used treatment for WM. Almost all of the recommended systemic therapy regimens include Rituxan® and one or more chemotherapy medicines.

There are four systemic therapy regimens preferred by NCCN experts. See Guide 2 on the following page. While the regimens in Guide 2 are preferred, there are a number of other recommended regimens that are also appropriate choices for treatment. See Guide 3 on page 32.

Avoiding stem-cell toxic medicines
Some systemic therapy medicines can damage blood stem cells. While not a primary treatment for WM, a stem cell transplant may be an option for treating WM that returns more than once after primary treatment.
If there is even a small chance that you may have a stem cell transplant at some point in the future, your doctor will limit the use of systemic therapy regimens that could damage your stem cells. Stem cell damage could lead to other types of serious blood disorders unrelated to WM, such as leukemia.

Shingles prevention
Some systemic therapy medicines can reactivate the herpes zoster ("shingles") virus. Shingles is a painful skin rash caused by the same virus that causes chickenpox (varicella zoster). To reduce the risk of shingles, your doctor may ask you to get the shingles vaccine and/or take an antiviral medication called acyclovir before starting treatment with certain systemic therapy regimens.

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 27 for more information on clinical trials.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Pneumocystis pneumonia prevention needed</th>
<th>Shingles prevention needed</th>
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<th>Good to know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bendamustine and rituximab</td>
<td>✓</td>
<td>–</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>Bortezomib, dexamethasone, and rituximab</td>
<td>–</td>
<td>✓</td>
<td>✓</td>
<td>Avoid if you have nerve damage related to WM.</td>
</tr>
<tr>
<td>Ibrutinib with or without rituximab</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Works best in people with MYD88 mutation</td>
</tr>
<tr>
<td>Rituximab, cyclophosphamide, and dexamethasone</td>
<td>–</td>
<td>–</td>
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</table>
### Guide 3
#### Other recommended systemic therapy regimens and related care

<table>
<thead>
<tr>
<th>Regimen</th>
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</tr>
<tr>
<td>Bortezomib and dexamethasone</td>
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<td>√</td>
<td>√</td>
<td>Avoid if you have nerve damage related to WM.</td>
</tr>
<tr>
<td>Carfilzomib, rituximab, and dexamethasone</td>
<td>—</td>
<td>√</td>
<td>√</td>
<td>May cause heart or lung damage, especially in the elderly.</td>
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<tr>
<td>Cladribine with or without rituximab</td>
<td>—</td>
<td>√</td>
<td>—</td>
<td>May increase the risk of MDS/AML. Avoid if you may have a future stem cell transplant.</td>
</tr>
<tr>
<td>Cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab</td>
<td>—</td>
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<td>√</td>
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<td>Fludarabine with or without rituximab</td>
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<td>May increase the risk of MDS/AML. Avoid if you may have a future stem cell transplant.</td>
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<td>Fludarabine, cyclophosphamide, and rituximab</td>
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<td>Ixazomib, rituximab, and dexamethasone</td>
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<tr>
<td>Rituximab, cyclophosphamide, and prednisone</td>
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</table>
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 in large part 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 actually responding to treatment.

For example, rituximab 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.

A main goal of treating WM is to relieve symptoms. In addition to considering the IgM level, your doctor will consider whether you have any new or worsening symptoms of WM.

Possible responses to treatment

Cancer experts have developed criteria to determine how well WM responds to treatment. These response categories are also used to determine whether you need more treatment. See Guide 4.

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. 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 4–6 months for an additional 3 years, then every 6–12 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 systemic therapy that contained rituximab (Rituxan®), continuing treatment with rituximab alone as maintenance therapy is an option. Maintenance therapy may keep you cancer-free for longer.

Other responses to treatment

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 don't 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 4–6 months for 3 more years, then every 6–12 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 systemic therapy that contained rituximab (Rituxan®), continuing treatment with rituximab alone as maintenance therapy is an option. Maintenance therapy may keep you cancer-free for longer.
Stable or progressive disease
If there is no response to treatment, this means the IgM level stayed about the same. It is called stable disease. If the cancer does not respond to treatment or if symptoms persist or get worse, switching to a different systemic therapy regimen is recommended.

Guide 4
Response categories for WM

<table>
<thead>
<tr>
<th>Description</th>
<th>Next steps</th>
</tr>
</thead>
</table>
| **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  
• Maintenance therapy with rituximab (Rituxan)® (optional) |
| **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  | No symptoms:  
• Watch-and-wait  
• Monitor IgM  
• Maintenance therapy with rituximab (Rituxan)® (optional)  

If symptoms:  
• Switch to a different systemic therapy regimen |
| **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  |  |
| **Minor response** | • IgM level reduced by less than half  
• No new signs or symptoms of WM  |  |
| **Stable disease** | • 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  |  |
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 many other types of lymphomas.
Previously treated WM

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

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 systemic therapy regimen. This may be the case if primary treatment was very harsh or caused severe side effects. The systemic therapy regimens preferred by NCCN experts for previously treated WM are listed in Guide 5.

If you are a candidate for a stem cell transplant, it is important to avoid systemic therapy medicines that can damage stem cells. This is especially important if you haven’t had any stem cells harvested. Guide 5 indicates the systemic therapy regimens to avoid if you might have a stem cell transplant at some point.

While the regimens in Guide 5 are preferred, there are a number of other recommended regimens that are also appropriate choices for treating relapsed WM. See Guide 6.

Guide 5
Preferred systemic therapy regimens for previously treated WM

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### Guide 6
Other recommended systemic therapy regimens for previously treated WM

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<td>Everolimus</td>
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<td>–</td>
<td>✓</td>
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</table>
If you can't have rituximab
Most of the systemic therapy regimens recommended for previously treated WM include rituximab (Rituxan®). Another anti-CD20 therapy called ofatumumab (Arzerra®) is an option for people who cannot have rituximab.

Like rituximab, ofatumumab can cause the level of IgM in the blood to increase by 25 percent or more. This is called IgM flare. IgM flare can lead to hyperviscosity, which can cause serious side effects. It can also cause IgM-related neuropathy, cryoglobulinemia, and other IgM-related complications to get worse. If IgM levels stay high while taking ofatumumab, it doesn't mean that treatment isn't working. It simply means that your doctor may need to take steps to offset or counteract the effects of IgM flare. Plasmapheresis is the best way to reduce hyperviscosity and its side effects.

If the level of IgM is high before starting treatment with ofatumumab, your doctor may recommend having plasmapheresis first. The goal is to help prevent symptomatic hyperviscosity before it starts.

Stem cell transplant
A stem cell transplant may be an option for some people with relapsed WM. The type of stem cell transplant recommended is called high-dose therapy with autologous stem cell rescue. This type of stem cell transplant uses your own healthy stem cells, not stem cells from a donor.

According to NCCN experts, an allogeneic stem cell transplant—which uses stem cells from a donor—should only be done as part of a clinical trial.
Review

- Systemic therapy is used to treat Waldenström macroglobulinemia (WM) that is causing symptoms.
- Most of the recommended systemic therapy regimens include a targeted therapy called rituximab (Rituxan®).
- People who may have a stem cell transplant at some point in the future should avoid systemic therapy medicines that can damage stem cells.
- 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 after primary treatment.
4
Making treatment decisions

41 It’s your choice
41 Questions to ask your doctors
44 Websites
It’s 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 can’t be ignored, there may be 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 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 doctors

Possible questions to ask your doctors are on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.
What's my diagnosis and prognosis?

Your doctor should clearly explain the type of cancer you have. This is your diagnosis. Your doctor should also be able to tell you how he or she expects your cancer to respond to treatment. This is your prognosis.

1. Where did the cancer start?
2. Is this cancer common?
3. What is the cancer stage? Does this stage mean the cancer has spread far?
4. What other test results are important to know?
5. How often are these tests wrong?
6. Would you give me a copy of the pathology report and other test results?
7. How likely is it that I'll be cancer-free after treatment?
What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option, along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Are you suggesting options other than what NCCN recommends? If yes, why? What are these other options based on?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options?
7. Which option is proven to work best? Which options lack scientific proof?
8. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Less time-consuming? Less expensive?
9. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
10. What can be done to prevent or relieve the side effects of treatment?
11. What are my chances that the cancer will return?
12. How soon should I start treatment? If there are delays in starting my treatment, how will this impact my treatment options?
**Websites**

**American Cancer Society**
cancer.org/cancer/waldenstrom-macroglobulinemia/about/what-is-wm.html

**International Waldenstrom’s Macroglobulinemia Foundation (IWMF)**
iwmf.com

**National Cancer Institute**
cancer.gov/types/lymphoma/patient/adult-nhl-treatment-pdq

**The Leukemia & Lymphoma Society**
lls.org/

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

**U.S. National Library of Medicine Genetics Home Reference**
ghr.nlm.nih.gov/condition/waldenstrom-macroglobulinemia
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.

**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**
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 medical tests and treatments 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 dye put into your body to make clearer pictures during imaging tests.

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

**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.

**immunohistochemistry (IHC)**
A test of cancer cells to find specific cell traits involved in abnormal cell growth.

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

**lymph**
A clear fluid containing 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.
**Words to know**

**lymphocyte**
A type of immune cell that is made in the bone marrow and is found in the 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.

**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.

**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**
The use of medicines that can target and attack cancer cells.

**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 1.2020. It was adapted, reviewed, and published with help from the following people:

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