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Treating Waldenstrom Macroglobulinemia

If you've been diagnosed with Waldenstrom macroglobulinemia, your treatment team will discuss your options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is Waldenstrom macroglobulinemia treated?

If treatment is needed for Waldenstrom macroglobulinemia (WM), several types can be used:

- [Chemotherapy for Waldenstrom Macroglobulinemia](#)
- [Targeted Drug Therapy for Waldenstrom Macroglobulinemia](#)
- [Biological Therapy or Immunotherapy for Waldenstrom Macroglobulinemia](#)
- [Plasmapheresis \(Plasma Exchange\) for Waldenstrom Macroglobulinemia](#)
- [Stem Cell Transplant for Waldenstrom Macroglobulinemia](#)
- [Radiation Therapy for Waldenstrom Macroglobulinemia](#)

Common treatment approaches

them to see which ones are best. Because of this, there is no single standard treatment for all patients.

- [When to Treat People with Waldenstrom Macroglobulinemia](#)

Who treats Waldenstrom macroglobulinemia?

Based on your treatment options, you might have different types of doctors on your treatment team:

- A **hematologist**: a doctor who treats disorders of the blood, including lymphomas such as WM
- A **medical oncologist**: a doctor who treats cancer with chemotherapy and other medicines
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy

Many other specialists might be part of your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, nutrition specialists, social workers, and other health professionals.

- [Health Professionals Associated with Cancer Care](#)

Making treatment decisions

It's important to discuss all treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. You may feel that you need to make a decision quickly, but it's important to give yourself time to absorb the information you have learned. Ask your cancer care team questions.

If time permits, it is often a good idea to seek a second opinion, particularly for a rare condition such as Waldenstrom macroglobulinemia. A second opinion may give you more information and help you feel more confident about the treatment plan you choose.

- [Questions to Ask About Waldenstrom Macroglobulinemia](#)
- [Seeking a Second Opinion](#)

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the-art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

- [Clinical Trials](#)

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your r0 0 0Tm /F3 viw0 0 1 72 4

important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

- [Palliative Care](#)
- [Programs & Services](#)

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors and you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

- [If Cancer Treatments Stop Working](#)

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Chemotherapy for Waldenstrom Macroglobulinemia

Chemo drugs attack cells that are dividing quickly, which is why they work against WM cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to certain side effects.

The side effects of chemo depend on which drugs are used, the doses, and the length of time they are taken. Common side effects include:

- Nausea and vomiting
- Loss of appetite
- Hair loss
- Mouth sores
- Diarrhea or constipation
- Increased risk of infections (from having too few white blood cells)
- Problems with bleeding or bruising (from having too few blood platelets)
- Fatigue (tiredness) and shortness of breath (from having too few red blood cells)

Other side effects can be seen with certain drugs. For example, doxorubicin can damage the heart. Corticosteroid drugs can cause problems sleeping and an increased appetite.

If you have side effects, your cancer care team can suggest steps to ease them. For example, medicines can be taken to help prevent and control nausea and vomiting. Most side effects are temporary and go away after treatment is finished. If you have serious side effects, the chemo may have to be reduced or stopped, at least temporarily.

Long-term side effects of chemotherapy

Some chemo drugs cause long-term side effects that can affect almost any part of the body. One of the most serious complications with certain chemo drugs is the possibility of developing leukemia later on. It affects a very small percentage of patients, but it is more common in patients who take fludarabine or alkylating agents.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see [Chemotherapy](#)¹

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)².

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
2. www.cancer.org/cancer/managing-cancer/side-effects.html
www.cancer.org/cancer/types/waldenstrom-macroglobr4pfects.

Targeted Drug Therapy for Waldenstrom

Macroglobulinemia

- [Bruton tyrosine kinase \(BTK\) inhibitors](#)
- [Proteasome inhibitors](#)
- [mTOR inhibitors](#)
- [More information about targeted therapy](#)

As researchers have learned more about the changes inside cells that cause cancer, they have developed newer drugs that target these changes. These are often referred to as **targeted therapy drugs**. These drugs work differently from standard [chemotherapy](#) (chemo) drugs. They sometimes work when chemo drugs don't, and they often have different side effects.

Bruton tyrosine kinase (BTK) inhibitors

Ibrutinib (Imbruvica) and **zanubrutinib (Brukinsa)** block a protein called Bruton tyrosine kinase (BTK) inside lymphoma cells, which normally helps the cells grow and survive. Ibrutinib can be used alone or in combination with [rituximab](#) to treat WM, while zanubrutinib is typically used by itself. These drugs are taken by mouth as pills, typically once or twice a day.

Common side effects of BTK inhibitors include diarrhea, rash, muscle and bone pain, fatigue, cough, bruising, and low blood cell counts. More serious side effects can include bleeding, serious infections, and heart rhythm problems. Some people taking these drugs develop skin or other cancers, so it's important to use sun protection when outside while taking one of these drugs.

Proteasome inhibitors

These drugs stop enzyme complexes (proteasomes) inside cells from breaking down proteins that normally help keep cell division under control.

Bortezomib (Velcade) and **carfilzomib (Kyprolis)** are sometimes helpful in treating WM. These drugs are given as an infusion into a vein (IV); bortezomib can also be given as an injection under the skin (sub-q).

Although these drugs work slightly differently from most chemo drugs, they can still cause many of the same types of [side effects](#)¹, including low blood counts, nausea, and loss of appetite. They can also damage nerves, causing pain in the feet and legs

Biological Therapy or Immunotherapy for Waldenstrom Macroglobulinemia

- [More information about immunotherapy](#)

Biological therapies help the body's immune system fight the cancer or use man-made versions of substances normally made by the immune system. These substances can kill Waldenstrom macroglobulinemia (WM) cells or slow their growth.

Monoclonal antibodies

Antibodies are proteins made by the immune system to help fight infections. Man-made versions, called **monoclonal antibodies**, can be designed to attack a specific target, such as a substance on the surface of lymphocytes (the cells in which WM starts).

Rituximab (Rituxan) is the most widely used monoclonal antibody for WM. It attaches to a protein called CD20 on the surface of lymphoma cells. This attachment tells the lymphoma cell to die. Patients get rituximab by infusion into a vein (IV) at the doctor's office or clinic. Rituximab can be given alone or with chemotherapy or targeted therapy (or other drugs) as a part of treatment.

This drug has to be given carefully to WM patients because sometimes it can actually raise the level of IgM in the blood at first, which can lead to problems with hyperviscosity (thickened blood). Side effects during the infusion are common, and can include chills, fever, nausea, rashes, fatigue, and headaches. Unlike regular chemotherapy, rituximab does not cause low blood counts or hair loss.

Ofatumumab (Arzerra) is another antibody that targets the CD20 antigen. It can be used for people who have trouble taking rituximab. Side effects are similar to those seen with rituximab, including an increased risk of IgM levels going up when the drug is first given.

boosting parts of your immune system, although exactly how they work is not clear. These drugs are most often used to treat [multiple myeloma](#)², but they might also be

1. www.cancer.org/cancer/types/chronic-lymphocytic-leukemia.html
2. www.cancer.org/cancer/types/multiple-myeloma.html
3. www.cancer.org/cancer/managing-cancer/side-effects/nervous-system/peripheral-neuropathy.html
4. www.cancer.org/cancer/managing-cancer/cancer-drugs.html
5. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
6. www.cancer.org/cancer/managing-cancer/side-effects.html
7. www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html

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[See all references for Waldenstrom Macroglobulinemia](#)

Last Revised: November 30, 2018

Plasmapheresis (Plasma Exchange) for Waldenstrom Macroglobulinemia

If the level of abnormal IgM protein in the blood gets very high in a patient with Waldenstrom macroglobulinemia (WM), the blood becomes very thick (viscous). This is called **hyperviscosity syndrome** and can lead to brain damage (like a stroke) and bleeding problems. When this happens, the level of IgM needs to be lowered right away.

Plasmapheresis (also known as **plasma exchange**) uses a machine to separate the plasma (the liquid part of blood) that contains the abnormal IgM protein from the blood cells. The plasma containing the abnormal protein is discarded, while the blood cells are mixed with salt solution and plasma from a donor and given back to the patient.

Plasmapheresis is done over a few hours while the person lies in a bed or sits in a reclining chair. The blood is removed through an IV line (usually in a vein in the arm), goes through the machine where the plasma is replaced, and then is returned to the body through another IV line. Sometimes, minor surgery is done before the procedure to put a single large catheter in a large vein just below the neck or under the collar bone instead of using IV lines in the arms. This type of catheter, called a [central line or central venous catheter \(CVC¹\)](#), has both IVs built in.

Plasmapheresis is not painful (aside from the IV lines being put in), but it can be hard to stay sitting or lying down in the same place for 2 or 3 hours. Calcium levels can drop in some people during treatment, causing numbness and tingling (especially in the hands and feet and around the mouth) and muscle spasms, which can sometimes be painful. This can be treated by giving the patient calcium.

Plasmapheresis works quickly to bring down the IgM level. However, it does not treat the cause of the high IgM level (the cancer cells themselves), so it will go back up again without further treatment (like chemotherapy). Plasmapheresis is usually given to help the patient until chemotherapy or other drugs have a chance to work. It can also be used in people whose WM is not controlled by other [treatments](#).

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-

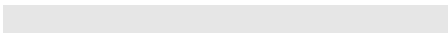
[ports-catheters.html](#)

2. www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html

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Stem Cell Transplant for Waldenstrom Macroglobulinemia



In an allogeneic SCT, the stem cells for the transplant come from someone else (a donor). The donor's tissue type (also known as the HLA type) needs to match the patient's tissue type as closely as possible to help prevent the risk of major problems with the transplant. Usually this donor is a brother or sister if they have the same tissue type as the patient. If there are no siblings with a good match, the cells may come from an HLA-matched, unrelated donor – a stranger who has volunteered to donate cells.

The stem cells for an allogeneic SCT are usually collected from a donor's bone marrow or blood on several occasions. Regardless of the source, the stem cells are then frozen and stored until they are needed for the transplant.

Allogeneic transplants have more risks and side effects than autologous transplants, so patients typically need to be younger and relatively healthy to be good candidates. Another challenge is that it can sometimes be difficult to find a matched donor.

One of the most serious complications of allogeneic SCTs is known as **graft-versus-host disease (GVHD)**. It happens when the patient's immune system is taken over by that of the donor. When this happens, the donor immune system may consider the patient's own body tissues to be foreign and attacks them.

Symptoms of GVHD can include severe skin rashes, itching, mouth sores (which can affect eating), nausea, and severe diarrhea. Liver damage can cause yellowing of the

Side effects from a stem cell transplant are generally divided into early and long-term effects.

Early or short-term effects: The early complications and side effects are basically the same as those caused by any other type chemotherapy, but they tend to be more severe.

One of the most common and serious short-term effects is the increased risk of [infection](#)³. Antibiotics are often given to try to keep this from happening. Other side effects, like low red blood cell and platelet counts, may require [blood product transfusions](#)⁴ or other treatments.

A possible side effect of allogeneic transplants is graft-versus-host disease, which is described above.

Long-term side effects: Some complications and side effects can remain for a long time or might not occur until months or years after the transplant. These include:

- Loss of fertility
- Damage to the thyroid gland
- Cataracts (damage to the lens of the eye)
- Damage to the lungs, causing shortness of breath
- Bone damage called aseptic necrosis (If damage is severe, the patient might need to have part of the affected bone and the joint replaced.)
- Development of another cancer (such as leukemia) years later

Things to consider before having a stem cell transplant

A stem cell transplant is a complex treatment that can cause life-threatening side effects because of the high doses of chemotherapy used. Be sure you understand the possible benefits and risks. If the doctors think you might benefit from a transplant, it should be done at a hospital where the staff has experience with the procedure and with managing the recovery. Some stem cell transplant programs might not have experience in certain types of transplants, especially transplants from unrelated donors.

SCTs often require a long hospital stay and can be very expensive (costing well over \$100,000). Because some insurance companies might view it as an experimental treatment, they might not pay for it. Even if the transplant is covered by your insurance, your co-pays or other costs could easily amount to tens of thousands of dollars. Find out what your insurer will cover before deciding on a transplant so you will have an idea of

what you might have to pay.

More information about stem cell transplant

To learn more about stem cell transplants, including how they are done and their potential side effects, see [Stem Cell Transplant for Cancer](#)⁵.

For more general information about side effects and how to manage them, see [Managing Cancer-related Side Effects](#)⁶.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/side-effects.html
2. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html
3. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/infections.html
4. www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html
5. www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-transplant.html
6. www.cancer.org/cancer/managing-cancer/side-effects.html
7. www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html

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[See all references for Waldenstrom Macroglobulinemia](#)

Last Revised: July 19, 2018

Radiation Therapy for Waldenstrom Macroglobulinemia

- [More information about radiation therapy](#)

Radiation therapy uses high-energy rays to kill cancer cells. This type of treatment is not used often to treat Waldenstrom macroglobulinemia (WM). Rarely, it is used to shrink an enlarged spleen or lymph nodes if they are causing symptoms.

The type of radiation therapy used to treat WM is called **external beam radiation**. The treatment is much like getting an x-ray, but the radiation is much stronger. The procedure itself is painless. Before the treatments start, the radiation team takes careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. Each treatment lasts only a few minutes, although the setup time — getting you into place for treatment — usually takes longer. Most often, radiation treatments are given 5 days a week for a few weeks.

Possible side effects

Immediate side effects of radiation therapy can include sunburn-like skin problems, fatigue, and low blood cell counts. Other side effects depend on the area being treated.

Radiation of the abdomen may cause [nausea, vomiting](#)¹, or [diarrhea](#)². Radiation to the

Mazzucchelli M., Frustaci A.M., Deodato M., Cairoli R., Tedeschi A. Waldenstrom's macroglobulinemia: an update. *Mediterr J Hematol Infect Dis* 2018, 10(1): e2018004, DOI: <http://dx.doi.org/10.4084/MJHID.2018.004>

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[See all references for Waldenstrom Macroglobulinemia](#)

Last Revised: July 19, 2018

When to Treat People with Waldenstrom Macroglobulinemia

- [If treatment doesn't work or if the disease comes back after treatment](#)

Waldenstrom macroglobulinemia (WM) is generally not considered to be curable, but it is treatable. Many different medicines can help keep WM under control, often for long periods of time.

Not everyone with WM needs treatment right away. In fact, some people are diagnosed with WM before they even have symptoms from it. Most experts recommend that people with WM should not usually be treated until the disease is causing problems. This lets people avoid the side effects of [chemotherapy \(chemo\)](#), [targeted therapy](#), or [immunotherapy](#) drugs until they really need these medicines. In fact, studies suggest that patients who delay treatment until their WM is causing problems do not live any less time than those who start treatment as soon as they are diagnosed.

Doctors agree that **hyperviscosity syndrome** is a reason to treat with [plasmapheresis](#) right away, because it can be life threatening. Other reasons to start treatment include problems from amyloidosis or cryoglobulins, as well as anemia (too few red blood cells),

Other drugs and drug combinations can also be used. Talk to your doctor about which regimen might be best for you based on your situation.

During treatment, you'll have regular visits with your doctor, who will ask you about your symptoms, do physical exams, and test your blood to see how well the treatment is working. In most people with WM, the disease will respond to treatment (IgM levels will go down and symptoms will get better) within a few months, although this may take longer in people getting only rituximab . If the WM responds, options include close monitoring for signs of disease progression or giving rituximab on a regular schedule to help keep the disease in check.

If treatment doesn't work or if the disease comes back after treatment

No single treatment for WM works for all patients. If the first drug or set of drugs doesn't work, other drugs may be helpful.

Most people with WM will require treatment with different drugs at some point. Often, a certain drug or combination of drugs will work at first, but over time it might stop working. Or a person might stop treatment if the WM is under control, only to have it [come back](#)¹ some time later. If the WM remained under control for at least a year after the first treatment, then giving the same drug(s) again can often help bring the cancer back under control.

If the cancer comes back sooner, or if the initial treatment was not effective, then switching to another drug or drug combination is likely to be a better option. Many of the same drugs and combinations listed above as first-line treatments might be helpful here. Other drugs that might also be tried include alemtuzumab (Campath), ofatumumab (Arzerra), or everolimus (Afinitor). High-dose chemotherapy with stem cell transplant might also be an option for some patients.

If chemotherapy or other drugs are no longer slowing the growth of the WM, some patients can still get relief from symptoms by getting plasmapheresis at regular intervals to lower the levels of the abnormal IgM protein in their blood.

Sometimes WM can turn into an aggressive lymphoma. When this happens, the cancer grows much more quickly and causes symptoms that can soon become life threatening. These lymphomas are usually treated with a combination of several chemo drugs like those used for patients who are first diagnosed with an aggressive non-Hodgkin lymphoma (see [Treating Non-Hodgkin Lymphoma](#)²). If combination chemo is not

successful, high-dose chemo with a stem cell transplant may be an option.

Hyperlinks

1. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
2. www.cancer.org/cancer/types/non-hodgkin-lymphoma/treating.html
3. www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html

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