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Treating Non-Hodgkin Lymphoma

If you've been diagnosed with non-Hodgkin lymphoma, 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 non-Hodgkin lymphoma treated?

Depending on the type and stage (extent) of the lymphoma and other factors, treatment options for people with NHL might include:

- [Chemotherapy for Non-Hodgkin Lymphoma](#)
- [Immunotherapy for Non-Hodgkin Lymphoma](#)
- [Targeted Drug Therapy for Non-Hodgkin Lymphoma](#)
- [Radiation Therapy for Non-Hodgkin Lymphoma](#)
- [High-Dose Chemotherapy and Stem Cell Transplant for Non-Hodgkin Lymphoma](#)
- [Surgery for Non-Hodgkin Lymphoma](#)

Common treatment approaches

Treatment approaches for NHL depend on the type of cancer, how advanced it is, as well as your health and other factors.

Another important part of treatment for many people is palliative or supportive care. This can help prevent or treat problems such as infections, low blood cell counts, or some symptoms caused by the lymphoma.

- [Treating B-Cell Non-Hodgkin Lymphoma](#)
- [Treating T-Cell Non-Hodgkin Lymphoma](#)
- [Treating HIV-Associated Lymphoma](#)

- [Palliative and Supportive Care for Non-Hodgkin Lymphoma](#)

Who treats non-Hodgkin lymphoma?

Based on your treatment options, you may have different types of doctors on your treatment team. These doctors could include:

- A **medical oncologist** or **hematologist**: a doctor who treats lymphoma with chemotherapy, immunotherapy, and targeted therapy.
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy.
- A **bone marrow transplant doctor**: a doctor who specializes in treating cancer or other diseases with bone marrow or stem cell transplants.

You might have many other specialists on your treatment team as well, including physician assistants, nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals.

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

Making treatment decisions

It's important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. In choosing a treatment plan, consider your health and the type and stage of the lymphoma.

It's also very important to ask questions if there is anything you're not sure about.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- [Questions to Ask About Non-Hodgkin Lymphoma](#)
- [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 regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- [Complementary and Integrative Medicine](#)

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an 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 Non-Hodgkin Lymphoma

Chemotherapy (chemo) is the use of anti-cancer drugs that are usually injected into a vein (IV) or taken by mouth. These drugs enter the bloodstream and reach almost all

areas of the body, making this treatment very useful for lymphoma.

When might chemo be used?

Chemo is the main treatment for most people with non-Hodgkin lymphoma (NHL). Depending on the [type](#)¹ and the [stage](#)² of the lymphoma, chemo may be used alone or combined with other treatments, such as [immunotherapy drugs](#) or [radiation therapy](#).

Which chemo drugs are used to treat non-Hodgkin lymphoma?

Many chemo drugs are useful in treating lymphoma. Often, several drugs are combined. The number of drugs, their doses, and the length of treatment depend on the type and stage of the lymphoma. Here are some of the drugs more commonly used to treat lymphoma (divided into groups based on how they work):

Alkylating agents

- Cyclophosphamide
- Chlorambucil
- Bendamustine
- Ifosfamide

Corticosteroids

- Prednisone
- Dexamethasone

Platinum drugs

- Cisplatin
- Carboplatin
- Oxaliplatin

Purine analogs

- Fludarabine
- Pentostatin
- Cladribine (2-CdA)

Anti-metabolites

- Cytarabine (ara-C)
- Gemcitabine
- Methotrexate
- Pralatrexate

Anthracyclines

- Doxorubicin (Adriamycin)
- Liposomal doxorubicin (Caelyx)

Others

- Vincristine
- Mitoxantrone
- Etoposide (VP-16)
- Bleomycin

Often drugs from different groups are combined. One of the most common combinations is called CHOP. This includes the drugs cyclophosphamide, doxorubicin (also known as hydroxydaunorubicin), vincristine (**O**ncovin) and **p**rednisone. Another common combination leaves out doxorubicin and is called CVP.

Chemo is often combined with an immunotherapy drug, especially rituximab (Rituxan).

Doctors give chemo in cycles, in which a period of treatment is followed by a period of rest to allow the body time to recover. Each chemo cycle generally lasts for several weeks. Most chemo treatments are given on an outpatient basis (in the doctor's office or clinic or hospital outpatient department), but some might require a hospital stay.

Sometimes a patient may get one chemo combination for several cycles and later

switch to a different one if the first combination doesn't seem to be working.

Intrathecal chemo

Most chemo drugs given systemically (IV or by mouth) can't reach the cerebrospinal fluid (CSF) and tissues around the brain and spinal cord. To treat lymphoma that might have reached these areas, chemo may also be given into the CSF. This is called *intrathecal chemo*. The chemo drugs most often used for intrathecal chemo are methotrexate and cytarabine.

Possible side effects

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long treatment lasts. Common side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infection (from a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (from a shortage of platelets)
- Fatigue and shortness of breath (from too few red blood cells)

These side effects usually go away after treatment is finished. If serious side effects occur, the dose of chemo may be reduced or treatment may be delayed.

There are often ways to lessen these side effects. For example, drugs can be given to prevent or reduce nausea and vomiting.

Certain chemo drugs can have other possible side effects. For example:

- Platinum drugs such as cisplatin can cause nerve damage (*neuropathy*), leading to numbness, tingling, or even pain in the hands and feet.
- Ifosfamide can damage the bladder. The risk of this can be lowered by giving it along with a drug called *mesna*.
- Doxorubicin can damage the heart. Your doctor may order a test of your heart function (like a MUGA scan or echocardiogram) before starting you on this drug.
- Bleomycin can damage lungs. Doctors often test lung function before starting

someone on this drug.

- Many chemo drugs can affect fertility (the ability to have children).
- Some chemo drugs can raise your risk of developing leukemia several years later.

Tumor lysis syndrome is a possible side effect when chemo is started, especially in patients with large or fast-growing lymphomas. Killing the lymphoma cells releases their contents into the bloodstream. This can overwhelm the kidneys, which can't get rid of all of these substances at once. This can lead to the build-up of certain minerals in the blood and even kidney failure. The excess minerals can lead to heart and nervous system problems. Doctors work to prevent this by giving the patient extra fluids and certain drugs, such as sodium bicarbonate, allopurinol, and rasburicase.

Ask your health care team about what side effects you can expect based on the specific drugs you will receive. Be sure to tell your doctor or nurse if you do have side effects, as there are often ways to help with them. For example, drugs can be given to prevent or reduce nausea and vomiting.

Other drugs used to treat lymphoma

Other types of drugs can also be useful in treating some types of lymphoma. These drugs work differently from standard chemo drugs. For example, immunotherapy and [targeted therapy](#) drugs are helpful for some lymphomas.

Mucosa-associated lymphoid tissue (MALT) lymphoma, which usually starts in the stomach, is linked to infection with the bacterium *H. pylori*. Treatment of this infection can often make the lymphoma go away. This is most often done with a combination of **antibiotics** along with drugs called **proton pump inhibitors**, which lower stomach acid levels.

In a similar way, splenic marginal zone B-cell lymphoma is sometimes linked to infection with the hepatitis C virus. Treating the infection with **anti-viral drugs** can sometimes shrink these lymphomas, or even make them go away.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see [Chemotherapy](#)³.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)⁴.

Hyperlinks

1. </content/cancer/en/cancer/non-hodgkin-lymphoma/about/types-of-non-hodgkin-lymphoma.html>
2. www.cancer.org/cancer/non-hodgkin-lymphoma/detection-diagnosis-staging/staging.html
3. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Immunotherapy for Non-Hodgkin Lymphoma

Immunotherapy is treatment that either boosts the patient's own immune system or uses man-made versions of the normal parts of the immune system to kill lymphoma cells or slow their growth.

Monoclonal antibodies

Antibodies are proteins made by your 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 lymphomas start).

Several monoclonal antibodies are now used to treat non-Hodgkin lymphoma (NHL).

Antibodies that target CD20

A number of monoclonal antibodies target the CD20 antigen, a protein on the surface of B lymphocytes. These include:

- **Rituximab (Rituxan):** This drug is often used along with [chemotherapy](#) (chemo) for some types of NHL, but it may also be used by itself.
- **Obinutuzumab (Gazyva):** This drug is often used along with chemo as a part of the treatment for small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL). It can also be used along with chemo in treating follicular lymphoma.
- **Ofatumumab (Arzerra):** This drug is used mainly in patients with SLL/CLL that is no longer responding to other treatments.
- **Ibritumomab tiuxetan (Zevalin):** This drug is made up of a monoclonal antibody that is attached to a radioactive molecule. The antibody brings radiation directly to the lymphoma cells.

These drugs are given into a vein (IV), often over several hours. They all can cause reactions during the infusion (while the drug is being given) or several hours afterward. Most reactions are mild, such as itching, chills, fever, nausea, rashes, fatigue, and headaches. More serious reactions can include chest pain, heart racing, swelling of the face and tongue, cough, trouble breathing, feeling dizzy or lightheaded, and feeling

faint. Because of these kinds of reactions, drugs to help prevent them are given before each infusion.

There is also a form of rituximab called **rituximab and hyaluronidase injection (Rituxan Hycela)** that is given as a shot under the skin. It can take 5-7 minutes to inject the drug, but this is much shorter than the time it normally takes to give the drug by vein. It is approved for use in patients with follicular lymphoma, diffuse large B-cell lymphoma, and chronic lymphocytic leukemia. Possible side effects include local skin reactions, like redness, where the drug is injected, infections, low white blood cell counts, nausea, fatigue, and constipation.

Rituxan was the original brand name for rituximab, but several similar versions (called [biosimilars](#)¹) are now available as well, including Ruxience, Truxima, and Riabni.

All of these drugs can cause inactive hepatitis B infections to become active again, which can lead to severe or life-threatening liver problems. Your doctor may check your blood for signs of an old hepatitis B infection before you start treatment. These drugs can also increase your risk of certain serious infections for many months after the drug is stopped. Other side effects can depend on which drug is given. Ask your doctor what you can expect.

Antibodies that target CD19

Tafasitamab (Monjuvi) is an antibody directed at the CD19 antigen, a protein on the surface of B lymphocytes. This drug can be used along with lenalidomide (see Immunomodulating drugs, below) to treat diffuse large B-cell lymphoma (DLBCL) that has come back or is no longer responding to other treatments, in people who can't have a [stem cell transplant](#) for some reason.

This drug is infused into a vein (IV), typically about once a week for the first few months, and then once every two weeks.

Some people have infusion reactions while getting this drug, which can cause symptoms like chills, flushing, headache, or shortness of breath during the infusion. You'll likely get medicines before treatment to help lower this risk, but it's important to tell your healthcare provider right away if you have any of these symptoms.

Other side effects can include low blood cell counts (with an increased risk of bleeding and serious infections), feeling tired or weak, loss of appetite, diarrhea, cough, fever, and swelling in the hands or legs.

Antibody-drug conjugate with CD19 antibody

An antibody-drug conjugate (ADC) is a monoclonal antibody linked to a chemotherapy drug. In this case, the antibody directed against CD19 acts like a homing signal by attaching to the CD19 protein on cancer cells, bringing the chemo directly to them.

Loncastuximab tesirine (Zynlonta): This antibody-drug conjugate is used by itself to treat some types of large B-cell lymphoma (including diffuse large B-cell lymphoma, or DLBCL) after at least 2 other treatments (not including surgery or radiation) have been tried. This drug is given in a vein (IV) every 3 weeks.

Common side effects include abnormal liver function tests, low blood counts, feeling tired, rash, nausea, and muscle and joint pain. More serious side effects include infection, fluid collection in the lungs, around the heart, or in the abdomen (belly), very low blood counts, and very severe skin reactions when out in the sun.

Antibodies targeting CD52

Alemtuzumab (Campath) is an antibody directed at the CD52 antigen. It is useful in some cases of SLL/CLL and some types of peripheral T-cell lymphomas. This drug is infused into a vein (IV), usually 3 times a week for up to 12 weeks.

The most common side effects are fever, chills, nausea, and rashes. It can also cause very low white blood cell counts, which increases the risk for serious infections. Antibiotic and antiviral medicines are given to help protect against them, but severe and even life-threatening infections can still occur. Rare but serious side effects can include strokes, as well as tears in the blood vessels in the head and neck.

Antibodies that target CD30

Brentuximab vedotin (Adcetris) is an anti-CD30 antibody attached to a chemotherapy drug (an *antibody-drug conjugate*). The antibody acts like a homing signal, bringing the chemo drug to lymphoma cells, where it enters the cells and kills them.

Brentuximab can be used to treat some types of T-cell lymphoma, either as the first treatment (typically along with chemo) or if the lymphoma if it has come back after other treatments. This drug is infused into a vein (IV), typically every 3 weeks.

Common side effects can include nerve damage (neuropathy), low blood counts, fatigue, fever, nausea and vomiting, infections, diarrhea, and cough.

Antibodies that target CD79b

Polatuzumab vedotin (Polivy) is an anti-CD79b antibody attached to a chemotherapy drug (an *antibody-drug conjugate*). The antibody finds the lymphoma cell and attaches to the surface protein CD79b. Once connected, it is drawn into the lymphoma cell where the chemo is released and destroys it.

This drug can be used with bendamustine and rituximab to treat DLBCL, if the lymphoma has come back after receiving two other treatments. This drug is infused into a vein (IV), typically every 3 weeks.

Common side effects can include numbness or tingling of hands/feet ([peripheral neuropathy](#)²), low blood counts, fatigue, fever, decreased appetite, diarrhea, and pneumonia.

Immune checkpoint inhibitors

Immune system cells normally have substances that act as checkpoints to keep them from attacking other healthy cells in the body. Cancer cells sometimes take advantage of these checkpoints to avoid being attacked by the immune system.

Drugs such as **pembrolizumab (Keytruda)** work by blocking these checkpoints, which can boost the immune response against cancer cells. Pembrolizumab can be used to treat primary mediastinal large B-cell lymphoma (PMBCL) that has not responded to or has come back after other therapies.

Immunomodulating drugs

Drugs such as **thalidomide (Thalomid)** and **lenalidomide (Revlimid)** are thought to work against certain cancers by affecting parts of the immune system, although exactly how they work isn't clear. They are sometimes used to help treat certain types of lymphoma, usually after other treatments have been tried. Lenalidomide can be given with or without rituximab, or along with tafasitamab.

These drugs are taken daily as pills.

Side effects of can include low white blood cell counts (with an increased risk of infection) and neuropathy (painful nerve damage), which can sometimes be severe and may not go away after treatment. There is also an increased risk of serious blood clots (that start in the leg and can travel to the lungs), especially with thalidomide. Thalidomide can also cause drowsiness, fatigue, and severe constipation.

These drugs can cause severe birth defects if taken during pregnancy. Given this risk, the company that makes these drugs puts restrictions on access to them to prevent women who are or might become pregnant from being exposed to them.

Chimeric antigen receptor (CAR) T-cell therapy

In this treatment, immune cells called T cells are removed from the patient's blood and altered in the lab to have specific receptors (called *chimeric antigen receptors*, or CARs) on their surface. These receptors can attach to proteins on the surface of lymphoma cells. The T cells are then multiplied in the lab and given back into the patient's blood, where they can seek out the lymphoma cells and launch a precise immune attack against them.

Axicabtagene ciloleucel (Yescarta, also known as axi-cel) is a type of CAR T-cell therapy approved to treat people with:

- Large B-cell lymphoma (including diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and diffuse large B-cell lymphoma arising from follicular lymphoma) that hasn't responded to initial treatment with chemotherapy plus immunotherapy, or that comes back within a year of this treatment.
- Follicular lymphoma, diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and diffuse large B-cell lymphoma arising from follicular lymphoma, after at least two other kinds of treatment have been tried.

Tisagenlecleucel (Kymriah, also known as tisa-cel) is approved to treat people with diffuse large B-cell lymphoma, high grade B-cell lymphoma, and diffuse large B-cell lymphoma arising from follicular lymphoma, as well as follicular lymphoma that hasn't responded to or has come back after other therapies, after trying at least two other kinds of treatment.

Lisocabtagene maraleucel (Breyanzi, also known as liso-cel) is approved to treat adults with diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and follicular lymphoma grade 3B, after at least one other kind of treatment has been tried.

Brexucabtagene autoleucel (Tecartus, also known as brexu-cel) is approved to treat adults with mantle cell lymphoma that has come back or is no longer responding to other treatments.

Side effects of CAR T-cell therapy

Because CAR T-cell therapy can have serious side effects, it is only given in medical centers that have special training with this treatment.

- These treatments can sometimes cause **cytokine release syndrome (CRS)**, in which immune cells in the body release large amounts of chemicals into the blood. Symptoms of this life-threatening syndrome can include fever, chills, headache, nausea and vomiting, trouble breathing, very low blood pressure, a very fast heart rate, swelling, diarrhea, feeling very tired or weak, and other problems.
- These treatments can also sometimes cause serious **neurological (nervous system) problems**, such as confusion, trouble speaking, seizures, tremors, or changes in consciousness.
- Other serious side effects of these treatments can include **severe infections, low blood cell counts**, and a **weakened immune system**.

To learn more, see [CAR T-Cell Therapies](#)³.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see [Cancer Immunotherapy](#)⁴.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)⁵.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/biosimilar-drugs.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/peripheral-neuropathy.html
3. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html
4. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html
5. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Targeted Drug Therapy for Non-Hodgkin Lymphoma

As researchers have learned more about the changes in lymphoma cells that help them grow, they have developed newer drugs to specifically target these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. Sometimes they work when standard chemo drugs don't, and they often have different types of side effects.

Types of targeted drugs

- [Proteasome inhibitors](#)
- [Histone deacetylase \(HDAC\) inhibitor](#)
- [BTK inhibitors](#)
- [PI3K inhibitors](#)
- [EZH2 inhibitor](#)
- [Nuclear export inhibitor](#)

Proteasome inhibitors

These drugs work by stopping enzyme complexes (proteasomes) in cells from breaking down proteins important for keeping cell division under control. They are more often used to treat multiple myeloma, but can be helpful in treating some types of non-Hodgkin lymphoma (NHL) as well.

Bortezomib (Velcade) is a proteasome inhibitor used to treat some lymphomas, usually after other treatments have been tried. Bortezomib is given as an infusion into a vein (IV) or an injection under the skin (subcutaneous, or sub-q), typically twice a week for 2 weeks, followed by a rest period.

Side effects can be similar to those of standard chemo drugs, including low blood counts, nausea, loss of appetite, and nerve damage.

Histone deacetylase (HDAC) inhibitor

HDAC inhibitors are drugs that can affect what genes are active by interacting with proteins in chromosomes called *histones*.

Belinostat (Beleodaq) can be used to treat peripheral T-cell lymphomas, usually after at least one other treatment has been tried. It is given as an IV infusion, usually daily for 5 days in a row, repeated every 3 weeks.

Common side effects include nausea, vomiting, tiredness, and low red blood cell counts (anemia).

BTK inhibitors

Bruton's tyrosine kinase (BTK) is a protein that normally helps some lymphoma cells (B cells) to grow and survive. Drugs that target this protein, known as *BTK inhibitors*, can be helpful in treating some types of B-cell non-Hodgkin lymphomas.

These drugs are taken by mouth as capsules or tablets, typically once or twice a day.

Ibrutinib (Imbruvica) can be used to treat several types of NHL, including mantle cell lymphoma, marginal zone lymphoma, and small lymphocytic lymphoma. This drug is most often used after other treatments have been tried, although it's now being studied for use earlier in treatment.

Acalabrutinib (Calquence) can be used to treat mantle cell lymphoma (typically after at least one other treatment has been tried), as well as small lymphocytic lymphoma.

Zanubrutinib (Brukinsa) can be used to treat mantle cell lymphoma or marginal zone lymphoma, typically after at least one other treatment has been tried.

Common side effects of BTK inhibitors can include headache, diarrhea, bruising, fatigue, muscle pain, cough, rash, and low blood cell counts. Less common but more serious side effects can include bleeding (hemorrhage), infections, and heart rhythm problems (such as atrial fibrillation). These drugs may also increase the risk of skin or other cancers, so it's important to use sun protection when outside while taking one of these drugs.

PI3K inhibitors

Phosphatidylinositol 3-kinases (PI3Ks) are a family of proteins that send signals in cells

that can affect cell growth. Drugs that target these proteins, known as *PI3K inhibitors*, can be helpful in treating some types of non-Hodgkin lymphoma.

Copanlisib (Aliqopa) mainly targets the PI3K-alpha and PI3K-delta proteins. This drug can be used to treat follicular lymphoma, typically after other treatments have been tried. It's given as an infusion into a vein, typically once a week for 3 weeks, followed by a week off.

Common side effects include high blood sugar levels, nausea, diarrhea, feeling weak, high blood pressure, low levels of white blood cells (with increased risk of infection), and low levels of blood platelets (with increased risk of bruising or bleeding). Less common side effects include infections, inflammation in the lungs, and severe skin reactions.

Duvelisib (Copiktra) blocks the PI3K-delta and PI3K-gamma proteins. This drug can be used to treat small lymphocytic lymphoma, typically after other treatments have been tried. It's a pill taken twice a day.

Common side effects include diarrhea, fever, fatigue, nausea, cough, pneumonia, belly pain, joint/muscle pain and rash. Low blood counts, including low red blood cell counts (anemia) and low levels of certain white blood cells (neutropenia) are also common. Less often, more serious side effects can occur, such as liver damage, severe diarrhea, lung inflammation (pneumonitis), serious allergic reactions, and severe skin problems.

EZH2 inhibitor

Tazemetostat (Tazverik) works by targeting EZH2, a protein known as a *methyltransferase* that normally helps some cancer cells grow. This drug can be used to treat follicular lymphomas with an *EZH2* gene mutation, after other treatments have been tried. Tazemetostat can also be used to treat follicular lymphomas without an *EZH2* mutation, if there are no other good treatment options available. This drug is taken as pills, typically twice a day.

The most common side effects of this drug include bone and muscle pain, feeling tired, nausea, belly pain, and cold-like symptoms. Tazemetostat can also increase the risk of developing some types of blood cancers.

Nuclear export inhibitor

The nucleus of a cell holds most of the cell's important substances needed to make the proteins the cell uses to function and stay alive. A protein called XPO1 helps carry other proteins from the nucleus to other parts of the cell to keep it working.

Selinexor (Xpovio) is a drug known as a *nuclear export inhibitor*. It works by blocking the XPO1 protein. When the diffuse large B-cell lymphoma (DLBCL) cell cannot move proteins outside of its nucleus, the lymphoma cell dies.

This drug is used in people with DLBCL whose cancer has come back or has been treated with and no longer responds to at least 2 other DLBCL drugs.

It is a pill that is taken on the first and third day of each week.

Common side effects include feeling tired, nausea, diarrhea, loss of appetite, weight loss, vomiting, constipation, and fever. Other more serious side effects can include low platelet counts, low white blood cell counts, low blood sodium levels, infection, dizziness, and more severe gastrointestinal symptoms.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see [Targeted Cancer Therapy](#)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/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Radiation Therapy for Non-Hodgkin Lymphoma

Radiation therapy uses high-energy rays to kill cancer cells.

When might radiation therapy be used for non-Hodgkin lymphoma?

Radiation might be used to treat non-Hodgkin lymphoma (NHL) in some different situations:

- It can be used as the main treatment for some types of NHL if they are found early (stage I or II), because these tumors respond very well to radiation.
- For more advanced lymphomas and for some lymphomas that are more aggressive, radiation is sometimes used along with chemotherapy.

- People who are getting a stem cell transplant may get radiation to the whole body along with high-dose chemotherapy, to try to kill lymphoma cells throughout the body.
- Radiation therapy can be used to ease (palliate) symptoms caused by lymphoma that has spread to internal organs, such as the brain or spinal cord, or when a tumor is causing pain because it's pressing on nerves.

How is radiation therapy given?

When radiation is used to treat NHL, it's most often done with a carefully focused beam of radiation, delivered from a machine outside the body. This is known as *external beam radiation*. External beam radiation treatment for NHL might include beams made of photons (most common), protons or electrons depending on the situation.

Before your treatment starts, your radiation team will take careful measurements to find the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session, called *simulation*, usually includes getting imaging tests such as CT or MRI scans.

Most often, radiation treatments are given 5 days a week for several weeks. The treatment is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer.

Radiation can also be given as a drug in some cases. (See [Immunotherapy for Non-Hodgkin Lymphoma](#) for more details.)

Possible side effects

The side effects of radiation therapy depend on where the radiation is aimed. **Common side effects** include:

- Skin changes in areas getting radiation, ranging from redness to blistering and peeling
- Feeling tired
- Nausea
- Diarrhea

Nausea and diarrhea are more common if the abdomen (belly) is treated with radiation.

Radiation given to several areas, especially after chemotherapy, can lower blood cell counts and increase the risk of infections.

Radiation to the head and neck area can lead to mouth sores and trouble swallowing. Some people later have problems with dry mouth.

Often these effects go away shortly after treatment is finished.

Side effects tend to be worse if radiation and chemotherapy are given together.

Radiation techniques are much more advanced and can limit the radiation exposure to nearby organs, but **long-term serious side effects** are possible:

- Radiation to the chest might damage the lungs and lead to trouble breathing. It can also affect the heart, and may increase the chance of a heart attack later on.
- Radiation to the neck can lead to thyroid problems later in life. This can lead to fatigue and weight gain.
- Side effects of brain radiation therapy may become serious 1 or 2 years after treatment and may include headaches and problems such as memory loss, personality changes, and trouble concentrating.
- Other types of cancer can form in the area that received radiation. For example, radiation to the chest may increase the risk of lung cancer (especially in people who smoke) and of breast cancer, but this is rare.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see [Radiation Therapy](#)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/treatment/treatments-and-side-effects/treatment-types/radiation.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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High-Dose Chemotherapy and Stem Cell Transplant for Non-Hodgkin Lymphoma

A stem cell transplant (also known as a bone marrow transplant) lets doctors give higher doses of chemotherapy, sometimes along with radiation therapy.

The doses of chemotherapy drugs are normally limited by the side effects these drugs

can cause. Higher doses can't be used, even if they might kill more cancer cells, because they would severely damage the bone marrow, where new blood cells are made.

But with a stem cell transplant, doctors can give high doses of chemo because the patient receives a transplant of blood-forming stem cells to restore the bone marrow afterwards.

Stem cell transplants are sometimes used to treat lymphoma patients who are in remission or who have a relapse during or after treatment. Although only a small number of people with lymphoma are treated with this therapy, this number is growing.

Types of stem cell transplants

There are 2 main types of stem cell transplants (SCTs) based on where the stem cells come from.

- In an **autologous stem cell transplant**, the patient's own stem cells are used. They are collected several times in the weeks before treatment. The cells are frozen and stored while the person gets treatment (high-dose chemo and/or radiation) and then are given back into the patient's blood by an IV (catheter in the vein).
- In an **allogeneic stem cell transplant**, the stem cells come from someone else (a donor). Usually this is a brother or sister, although the source may be an unrelated donor or umbilical cord blood. 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. Regardless of the source, the stem cells are frozen and stored until they are needed for the transplant.

Autologous SCTs are used more often than allogeneic SCTs to treat lymphoma. Still, using the patient's own cells may not be an option if the lymphoma has spread to the bone marrow or blood. If that happens, it may be hard to get a stem cell sample that is free of lymphoma cells.

Allogeneic transplants are used less often for lymphoma because they can have severe side effects that make them hard to tolerate, especially for patients who are older or who have other medical problems. It can also be hard to find a matched donor.

A stem cell transplant is a complex treatment that can cause life-threatening side effects. If the doctors think a person might benefit from a transplant, it should be done at

a cancer center where the staff has experience with the procedure and with managing the recovery phase.

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](#)¹.

For more general information about side effects and how to manage them, see [Managing Cancer-related Side Effects](#)².

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Surgery for Non-Hodgkin Lymphoma

Surgery is often used to get a biopsy sample to diagnose and classify a lymphoma, but it's rarely used as a form of treatment.

Rarely, surgery may be used to treat lymphomas that start in the spleen or in certain organs outside the lymph system, such as the thyroid or stomach, and that have not spread beyond these organs. But for treating lymphoma that's completely confined to one area, [radiation therapy](#) is usually preferred over surgery.

More information about Surgery

For more general information about surgery as a treatment for cancer, see [Cancer Surgery](#)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/treatment/treatments-and-side-effects/treatment-types/surgery.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Palliative and Supportive Care for Non-Hodgkin Lymphoma

For most people with non-Hodgkin lymphoma (NHL), treatment of the lymphoma itself is the main concern. But patients can also often benefit from care aimed at helping with problems related to the NHL and its treatment. For example, some people with NHL have problems with infections or low blood counts. Although treating the NHL may help these problems over time, other therapies may be needed as well.

Treatments to prevent infections

Antibiotics and anti-virals

Patients getting certain chemotherapy drugs (such as fludarabine and other purine

analog) and the antibody drug alemtuzumab (Campath) have a high risk of infections seen mainly in people with impaired immune systems, like infection with CMV (a virus) and Pneumocystis pneumonia (PCP, which is caused by a type of fungus). An anti-viral drug like acyclovir is often given to try to prevent CMV infections. To help prevent PCP, a sulfa antibiotic is often given (trimethoprim with sulfamethoxazole, which is also known by brand names such as Septra and Bactrim). Other treatments are available for people who are allergic to sulfa drugs.

Antibiotics and anti-viral drugs are also given to treat infections. Often, active infections require higher doses or different drugs than those used to prevent infections.

Intravenous immunoglobulin (IVIG)

Some people with NHL have low levels of antibodies (immunoglobulins) to fight infections. This can lead to lung and/or sinus infections that keep coming back. The level of antibodies in the blood can be checked with a blood test, and if it is low, antibodies from donors can be given into a vein (IV) to help prevent infections. This is called *intravenous immunoglobulin* or *IVIG*. IVIG is often given once a month at first, but may be able to be given less often based on blood tests of antibody levels.

For more information on infections, see [Infections in People With Cancer](#)¹.

Treatments for low blood counts

Low white blood cell count: White blood cells, especially a certain kind of white blood cell called *neutrophils*, are needed to fight infection. Having too few neutrophils (neutropenia) can lead to serious or even life threatening infections. If you become neutropenic from chemotherapy (chemo), you may be treated with injections of a white blood cell growth factor, such as filgrastim (Neupogen) or pegfilgrastim (Neulasta), to boost your neutrophil count. This lowers the risk of serious infections and can allow chemo to continue on time. If you are neutropenic and have signs or symptoms of infection (like a fever), you will be treated with antibiotics.

Low platelet count: Platelets help blood to clot, which stops bleeding. If platelet counts get very low, it can lead to serious bleeding. Transfusions of platelets can often help prevent this.

In NHL, low platelet counts can also be caused by the cells being destroyed by abnormal antibodies. This is called *immune thrombocytopenia*. Before diagnosing this, the doctor often needs to check the bone marrow to make sure that there isn't another cause for the low platelet counts. In immune thrombocytopenia, giving platelet

transfusions doesn't usually help because the antibodies just destroy the new platelets, too. This can be treated by drugs that affect the immune system, like corticosteroids and IVIG. Another option is to remove the spleen, since after the antibodies stick to the platelets, they are actually destroyed in the spleen. A third option is treatment with a drug that tells the body to make more platelets, like eltrombopag (Promacta) or romiplostim (Nplate).

Low red blood cell count: Some people develop low red blood cell counts (anemia) from NHL or its treatment. This can lead to feeling tired, lightheaded, or short of breath. Anemia that is causing symptoms can be treated with red blood cell transfusions. Drugs that boost red blood cell production can also be used, but these are linked to worse outcomes, and so are generally only used for people who decline blood transfusions.

In NHL, abnormal antibodies can also lower red blood cell counts. This is called *autoimmune hemolytic anemia* (AIHA). It can be treated with drugs that affect the immune system, like corticosteroids and IVIG. Removing the spleen is also an option. If the patient is being treated with the chemo drug fludarabine (Fludara) when the AIHA develops, the drug may be the cause, and so the fludarabine will be stopped.

Palliative care

Whether your lymphoma is being treated or not, it's important to have treatment to relieve your symptoms. This type of treatment, sometimes called *palliative care*, can be given along with cancer treatment as well as [if cancer treatment is no longer working²](#).

Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, when lymph nodes become enlarged, they may press on nerves and cause pain. Radiation therapy to these areas may help relieve the pain. You might also be given pain medicines, ranging from ibuprofen and similar drugs to more potent medicines such as opioids (like morphine).

Nausea and loss of appetite can be treated with drugs and high-calorie food supplements. If the lymphoma has spread to the lungs, you may get short of breath. Oxygen may be used to help treat this.

It's important that you tell your health care team about any symptoms you have, including any side effects from treatment. There are often ways to help control or lessen these symptoms. This is an important part of your overall treatment plan.

More information about palliative care

To learn more about how palliative care can be used to help control or reduce symptoms caused by cancer, see [Palliative Care](#)³.

To learn about some of the side effects of cancer or treatment and how to manage them, see [Managing Cancer-related Side Effects](#)⁴.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/infections.html
2. www.cancer.org/treatment/treatments-and-side-effects/planning-managing/if-cancer-treatments-stop-working.html
3. www.cancer.org/treatment/treatments-and-side-effects/palliative-care.html
4. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html

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Treating B-Cell Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is generally divided into 2 main types, based on whether it starts in B lymphocytes (B cells) or T lymphocytes (T cells).

There are many different types of B-cell lymphomas. Treatment usually depends both on the [type of lymphoma](#)¹ and the [stage \(extent\) of the disease](#)², but many other factors can be important as well.

Jump to a section

- [Diffuse large B-cell lymphoma](#)
- [Primary mediastinal B-cell lymphoma](#)
- [Follicular lymphoma](#)
- [Small lymphocytic lymphoma \(and chronic lymphocytic leukemia\)](#)
- [Mantle cell lymphoma](#)
- [Extranodal marginal zone B-cell lymphoma – mucosa-associated lymphoid tissue \(MALT\) lymphoma](#)
- [Nodal marginal zone B-cell lymphoma](#)
- [Splenic marginal zone B-cell lymphoma](#)
- [Burkitt lymphoma](#)
- [Lymphoplasmacytic lymphoma \(Waldenstrom macroglobulinemia\)](#)
- [Hairy cell leukemia](#)
- [Primary central nervous system \(CNS\) lymphoma](#)
- [Primary intraocular lymphoma \(lymphoma of the eye\)](#)

Diffuse large B-cell lymphoma

Diffuse large B-cell lymphoma (DLBCL) tends to grow quickly. Most often, the treatment is [chemotherapy](#) (chemo), usually with a regimen of 4 drugs known as CHOP

(cyclophosphamide, doxorubicin, vincristine, and prednisone), plus the [monoclonal antibody](#) rituximab (Rituxan). This regimen, known as R-CHOP, is most often given in cycles 3 weeks apart. Because this regimen contains the drug doxorubicin, which can damage the heart, it may not be suitable for patients with heart problems, so other chemo regimens may be used instead.

Stage I or II

For DLBCL that is only in 1 or 2 lymph node groups on the same side of the diaphragm (the thin muscle that separates the chest from the abdomen), R-CHOP is often given for 3 to 6 cycles, which might be followed by radiation therapy to the affected lymph node areas.

Stage III or IV

Most doctors will give 6 cycles of R-CHOP as first-line treatment. After several cycles, doctors may get imaging tests such as a PET/CT scan to see how well treatment is working. People who have a higher risk of the lymphoma coming back later in the tissues around the brain and spinal cord may be treated with chemo injected into the spinal fluid (called *intrathecal chemotherapy*). Another option is to give high doses of methotrexate intravenously. (This drug can pass into the spinal fluid.)

For younger patients with a higher risk of the lymphoma coming back based on the International Prognostic Index (IPI) score, [high-dose chemo followed by a stem cell transplant](#) might be an option. But it's not yet clear if transplants are better as the initial treatment. Most doctors feel that if a transplant is done as part of the first treatment, it should be done in a clinical trial.

If the lymphoma doesn't go away completely with treatment or if it recurs (comes back) after treatment, doctors will usually suggest another chemo regimen. Several different regimens can be used, and they may or may not include rituximab. If the lymphoma shrinks with this treatment, it might be followed by a stem cell transplant if possible, as it offers the best chance of curing the lymphoma. Stem cell transplants are not effective unless the lymphoma responds to chemo. Unfortunately, not everyone is healthy enough for a stem cell transplant.

Other options for DLBCL that is no longer responding to chemo might include some type of [immunotherapy](#) (such as CAR T-cell therapy or a monoclonal antibody) or a [targeted therapy drug](#) such as selinexor (Xpovio).

[Clinical trials](#)³ of new treatments may be another good option for some people.

DLBCL can be cured in about half of all patients, but the stage of the disease and the IPI score can have a large effect on this. Patients with lower stages have better survival rates, as do patients with lower IPI scores.

Primary mediastinal B-cell lymphoma

This lymphoma, which starts in the space between the lungs (the mediastinum), is treated like early stage diffuse large B-cell lymphoma. A common treatment is 6 courses of [chemo](#) with CHOP plus [rituximab](#) (R-CHOP). This may be followed by [radiation](#) to the mediastinum. Often a PET/CT scan is done after the chemo to see if there's any lymphoma remaining in the chest. If no active lymphoma is seen on the PET/CT, the patient may be observed without further treatment. If the PET/CT scan is positive (shows possible active lymphoma), radiation may be needed. Sometimes, the doctor will order a biopsy of the chest tumor to confirm that lymphoma is still present before starting radiation.

Another treatment option is 6 cycles of chemo with dose-adjusted etoposide, doxorubicin and cyclophosphamide with vincristine, prednisone and rituximab (DA-EPOCH-R), which typically does not require any radiation.

If the primary mediastinal B cell lymphoma comes back or does not respond to chemo, another chemo regimen (possibly with a [stem cell transplant](#)) or some type of [immunotherapy](#) such as CAR T-cell therapy or an immune checkpoint inhibitor may be an option.

Follicular lymphoma

This type of lymphoma often grows slowly and responds well to treatment, but it is very hard to cure. It often comes back after treatment, although it can take many years to do so. It's not always clear if the lymphoma needs to be treated right away, especially if the lymphoma isn't causing problems other than mildly swollen lymph nodes. Some people may never need treatment at all. For those who do, sometimes it might be years before treatment is needed.

Stage I and early-stage II

If treatment is needed for follicular lymphoma that is only in 1 lymph node group or in 2 nearby groups that are both above or below the diaphragm (the thin muscle separating the chest from the abdomen), the preferred treatment is [radiation therapy](#) to the lymph node areas affected by lymphoma (called *involved site radiation*). Other choices include

treatment with [chemo](#) plus a [monoclonal antibody](#) (rituximab [Rituxan] or obinutuzumab [Gazyva]), or rituximab alone, which might be followed by radiation therapy.

Stages III, IV, and most stage II bulky lymphomas

If treatment is needed, the most common option is a monoclonal antibody (rituximab or obinutuzumab) combined with chemo. The chemo can be a single drug (such as bendamustine) or a combination of drugs, such as the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone) regimens.

If some lymph nodes are very large from the lymphoma, radiation may be used to reduce symptoms. This is most often used for patients who are too sick to be treated with chemo.

The radioactive monoclonal antibody ibritumomab (Zevalin) is also an option for initial treatment, although this is more often used as a second-line treatment.

For patients who may not be able to tolerate more intensive chemo regimens, rituximab alone, rituximab with milder chemo drugs (such as chlorambucil or cyclophosphamide), or rituximab with lenalidomide may be good options.

If the lymphoma shrinks or goes away with the initial treatment, doctors may advise either close follow-up or further treatment. This might include continuing the monoclonal antibody (rituximab or obinutuzumab) for up to 2 years, or treatment with ibritumomab. Further treatment may lower the chance that the lymphoma will come back later and may help some patients live longer, but it can also have side effects.

If follicular lymphoma doesn't respond to the initial treatment or if it comes back later, it may be treated with different chemo drugs, [targeted drugs](#), [immunotherapy](#) (such as CAR T-cell therapy or a monoclonal antibody), or some combination of these. If the lymphoma responds to this treatment, a [stem cell transplant](#) may be an option.

A small portion of follicular lymphomas, known as *grade 3B lymphomas*, tend to grow quickly, more like diffuse large B-cell lymphoma (DLBCL). Some follicular lymphomas can also change (transform) into or return as DLBCL. For these lymphomas, your doctor will review which treatments you may have already had to decide which is the next best treatment option.

Small lymphocytic lymphoma (and chronic lymphocytic leukemia)

Small lymphocytic lymphoma (SLL) and chronic lymphocytic leukemia (CLL) are considered different versions of the same disease. The main difference is where the cancer cells are (the blood and bone marrow for CLL, and the lymph nodes and spleen for SLL). CLL and SLL tend to grow slowly, but they are very hard to cure.

Treatment for SLL is similar to that of CLL, which is described in detail in [Treating Chronic Lymphocytic Leukemia](#)⁴.

If the lymphoma isn't growing quickly or causing any problems, it can be watched closely without treatment for a time. If treatment is needed, it depends on the stage.

When the lymphoma is only in one lymph node or lymph node area (stage I), it may be treated with [radiation therapy](#) alone.

For more advanced disease, the treatment is often the same as what is used for CLL. (See [Treating Chronic Lymphocytic Leukemia](#)⁵.) [Chemo](#), with or without [rituximab](#) or [obinutuzumab \(Gazyva\)](#) is one option for first-line treatment. Chlorambucil, fludarabine, or bendamustine are some of the chemo drugs that are used. A [targeted drug](#) such as ibrutinib (Imbruvica) or acalabrutinib (Calquence) is another option, as is rituximab alone (without chemo). Which treatment is used depends on a person's age and health, as well as on whether the cancer cells have certain chromosome changes.

If the lymphoma doesn't respond or comes back after initial treatment, different chemo drugs, targeted drugs, and/or other monoclonal antibodies may be used as second-line treatment.

Mantle cell lymphoma

This type of lymphoma has often spread widely when it's first found. Although it doesn't usually grow as quickly as some other fast-growing lymphomas, it often doesn't respond as well to treatment, either. Because current treatments for this type of lymphoma aren't likely to cure it, patients might want to consider taking part in a [clinical trial](#)⁶.

If the lymphoma has only spread to 1 lymph node group or to 2 nearby groups on the same side of the diaphragm (stage I and some stage II), which is rare, it can sometimes be treated with [radiation therapy](#). Another option is to treat with [chemo](#) plus [rituximab](#).

Mantle cell lymphomas that have spread more widely when they are first diagnosed are treated with chemo plus rituximab.

When possible, the chemo treatment is intense, using regimens such as:

- Hyper-CVAD: cyclophosphamide, vincristine, doxorubicin (Adriamycin), and dexamethasone, alternating with high-dose methotrexate plus cytarabine)
- “Dose-intensified” R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), alternating with rituximab and cytarabine
- RDHAP (Rituximab, dexamethasone, cytarabine, cisplatin)

If the lymphoma responds well to these initial treatments, a [stem cell transplant](#) may be a good option, followed by rituximab for 3 years.

Less intense chemo regimens, such as bendamustine with rituximab, may be used for people who are older or who have other health issues.

For mantle cell lymphomas that don’t respond or that come back after initial treatment, chemo with drugs such as bendamustine, bortezomib (Velcade), cladribine, fludarabine, or lenalidomide (Revlimid) may be used, sometimes along with other chemo drugs or with rituximab. Other options include the use of a [targeted drug](#), such as ibrutinib (Imbruvica), acalabrutinib (Calquence), or zanubrutinib (Brukinsa), as well as the [CAR T-cell therapy](#) brexucabtagene autoleucel (Tecartus). Other targeted drugs such as venetoclax (Venclexta) and idelalisib (Zydelig) have also shown promising results in some early studies. Still, because second-line treatment is not always helpful, patients might want to consider entering a [clinical trial](#)⁷.

Extranodal marginal zone B-cell lymphoma – mucosa-associated lymphoid tissue (MALT) lymphoma

Gastric (stomach) MALT lymphoma, the most common type, often occurs as a result of a chronic infection with the bacterium *H. pylori*, and it often responds to treatment of the infection. Because of this, gastric lymphomas are treated differently from other lymphomas in this group.

Stages I and II gastric lymphoma in people who test positive for *H. pylori*

Early-stage gastric MALT lymphomas are treated with antibiotics combined with drugs that block acid secretion by the stomach (called *proton pump inhibitors*). Usually the drugs are given for 10 to 14 days. This may be repeated after a couple of weeks. Examination of the stomach lining using upper endoscopy (where a flexible tube with a viewing lens is passed down the throat and into the stomach) is then repeated at certain intervals to see if the *H. pylori* is gone and if the lymphoma has shrunk.

About 2 out of 3 of these lymphomas go away completely with antibiotic treatment, but it

can sometimes take several months to be effective. In cases where symptoms need to be relieved before the antibiotics take effect or where antibiotics don't shrink the lymphoma, [radiation therapy](#) to the area is often the preferred treatment. The [monoclonal antibody](#) rituximab may be another option.

Stages I and II gastric lymphoma in people who test negative for H. pylori

For these early-stage gastric MALT lymphomas, treatment is usually either [radiation therapy](#) to the stomach or [rituximab](#).

Stage III or IV gastric lymphoma

For more advanced gastric MALT lymphomas, which are rare, treatment is often similar to that for follicular lymphoma (see above). Lymphomas that are not growing quickly may be watched and not treated right away. If the lymphoma is large, is causing symptoms, or is growing, it can be treated with [radiation therapy](#) to the stomach, [rituximab](#), [chemo](#), chemo plus rituximab, or a [targeted drug](#) such as ibrutinib (Imbruvica) or zanubrutinib (Brukinsa). The chemo drugs used are the same as those used for follicular lymphoma, and may include single agents such as chlorambucil or fludarabine or combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone).

Non-gastric MALT lymphoma

For MALT lymphomas that start in sites other than the stomach (non-gastric lymphomas), treatment depends on the location of the lymphoma and how much it has spread. Early-stage lymphomas can often be treated with [radiation](#) to the area containing the lymphoma. In certain sites (such as the lungs, breast, or thyroid), surgery may be an option. For more advanced disease (stage III or IV), treatment is generally the same as for stage III and IV gastric MALT lymphoma and follicular lymphoma (see above).

Nodal marginal zone B-cell lymphoma

This rare type of lymphoma is generally slow growing (indolent), and it often doesn't need to be treated right away. If it does need treatment, it is usually treated the same way as follicular lymphoma (which also tends to grow slowly).

Stage I and early-stage II

If treatment is needed for lymphoma that is only in 1 lymph node group or in 2 nearby groups on the same side of the diaphragm (the thin muscle separating the chest from the abdomen), the preferred treatment is [radiation therapy](#) to the lymph node areas affected by lymphoma (called *involved site radiation*). Other choices include treatment with [rituximab \(Rituxan\)](#), [chemo](#), or both, which might be followed by radiation therapy.

Stages III, IV, and most stage II bulky lymphomas

If treatment is needed, the most common option is rituximab combined with chemo. The chemo can be a single chemo drug (such as bendamustine or fludarabine) or a combination of drugs, such as the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone) regimens. If the lymphoma shrinks, a total of 6 cycles of chemo plus rituximab is usually given.

Other options for initial treatment include rituximab alone or chemo alone (either one or several drugs). If some lymph nodes are very large from the lymphoma, radiation may be used to reduce symptoms. This is most often used for patients who are too sick to be treated with chemo.

The radioactive [monoclonal antibody](#) ibritumomab tiuxetan (Zevalin) is also an option for initial treatment, although this is more often used as a second treatment.

For patients who may not be able to tolerate more intensive (stronger) chemo regimens, rituximab alone, milder chemo drugs (such as chlorambucil or cyclophosphamide), or both may be good options.

If the lymphoma shrinks or goes away with the initial treatment, doctors may advise either close follow-up or further treatment. This might include either rituximab for up to 2 years or treatment with ibritumomab tiuxetan. Further treatment may lower the chance that the lymphoma will come back later and may help some patients live longer, but it can also have side effects.

If the lymphoma doesn't respond to the initial treatment or if it comes back later, it may be treated with different chemo drugs, [immunotherapy](#), [targeted drugs](#), or some combination of these. If the lymphoma responds to this treatment, a [stem cell transplant](#) may be an option.

Nodal marginal zone B-cell lymphoma can also change into a fast-growing diffuse large B-cell lymphoma (DLBCL), which would require more aggressive chemotherapy (see above).

Splenic marginal zone B-cell lymphoma

This is typically a slow-growing lymphoma. If it is not causing symptoms, it is often watched closely without treating it right away.

About 1 in 3 people with this type of lymphoma have chronic hepatitis C virus (HCV) infection. Treating the infection with anti-viral drugs can often cause these lymphomas to go into remission.

If that doesn't work, or if a person isn't infected with HCV, [surgery](#) to remove the spleen can sometimes lead to a long-term remission. This can be very helpful in relieving symptoms if the spleen is enlarged. Treatment with rituximab may be another option.

If the disease is more advanced or progresses, it's usually treated with [chemo](#) with or without [rituximab](#) (similar to what is used for advanced stage follicular lymphoma, which is described above). Another option might be a [targeted drug](#) such as ibrutinib (Imbruvica) or zanubrutinib (Brukinsa), or rituximab with lenalidomide.

Sometimes this lymphoma can transform into an aggressive large-cell lymphoma, which then requires more intensive chemo.

Burkitt lymphoma

This is a very fast-growing lymphoma that is similar to a type of acute lymphocytic leukemia. It is usually treated in the hospital with intensive chemo, which usually includes at least 5 chemo drugs. Rituximab may also be added. Some examples of chemo regimens used for this lymphoma include:

- **Hyper-CVAD** (cyclophosphamide, vincristine, doxorubicin [Adriamycin], and dexamethasone), alternating with methotrexate and cytarabine (ara-C)
- **CODOX-M** (cyclophosphamide, vincristine [Oncovin], doxorubicin, and high-dose methotrexate), alternating with **IVAC** (ifosfamide, etoposide [VP-16], and cytarabine [ara-C])
- **EPOCH** (etoposide, prednisone, vincristine [Oncovin], cyclophosphamide, and doxorubicin)

Because this lymphoma tends to invade the area around the brain and spinal cord, the chemo drug methotrexate is often given into the spinal fluid (called *intrathecal therapy*). This may not be needed if high-dose methotrexate is given as a part of the main chemotherapy regimen.

An important part of the initial treatment of this disease is making sure a person gets plenty of fluids, as well as drugs like allopurinol, to help prevent tumor lysis syndrome (described in [Chemotherapy for Non-Hodgkin Lymphoma](#)).

If the lymphoma doesn't go away or if it comes back after treatment, another chemo regimen might be tried. If the lymphoma goes into remission, the doctor might suggest a stem cell transplant.

Lymphoplasmacytic lymphoma (Waldenstrom macroglobulinemia)

The main treatment for this lymphoma is usually chemo or rituximab. For more detailed information see [Treating Waldenstrom Macroglobulinemia](#)⁸.

Hairy cell leukemia

This is a slow-growing lymphoma that tends to invade the spleen and lymph nodes as well as the blood. Patients without symptoms often don't need to be treated right away. When treatment is needed, most often the chemo drugs cladribine (2-CdA) or pentostatin are used. For more detailed information, see [Treating Chronic Lymphocytic Leukemia](#)⁹.

Primary central nervous system (CNS) lymphoma

This lymphoma begins in the brain or spinal cord. It often develops in older people or those with immune system problems caused by AIDS or drugs given to keep transplanted organs from being rejected.

Most patients are treated with [chemo](#) and/or [radiation](#). One problem with treating this disease is that most chemo drugs commonly used to treat lymphoma don't reach the brain when given intravenously (IV). For people in reasonably good health, high IV doses of the drug methotrexate have been shown to be the most effective treatment. This is given along with the drug leucovorin and IV fluids, which help limit serious side effects. Other chemo drugs, such as cytarabine, may be added. [Rituximab](#) may be added as well. For those who aren't able to tolerate this treatment, other, less intensive chemo regimens or radiation therapy alone may be tried.

An issue with radiation therapy to the brain, especially in older patients, is that it can often cause mental changes. Doctors limit the dose of radiation to try to lessen this problem.

If CNS lymphoma keeps growing or comes back after treatment, further options may include chemo (using different drugs), radiation therapy, or a [stem cell transplant](#) if the person is healthy enough.

Primary intraocular lymphoma (lymphoma of the eye)

Most often doctors treat these cancers with radiation therapy, chemotherapy (chemo), or a combination of the two.

[External beam radiation therapy](#) is given if the cancer is limited to the eye. Radiation to both eyes may be recommended if lymphoma is found in both eyes. Because these lymphomas are commonly linked with lymphoma of the brain (CNS lymphoma), they have sometimes already spread outside the eye or to the brain when the cancer is first diagnosed. If this is the case, radiation therapy to the brain and spinal cord may be included because it can help prevent the lymphoma from spreading there or help destroy cancer cells that are there but haven't been seen by imaging. Problems with thinking, concentration, and memory are possible side effects from radiation to the brain and spinal cord.

Depending on the type of lymphoma, [chemo](#) may be used alone or in combination with radiation therapy, especially if it has grown outside the eye or spread to other places in the body. Chemo can be given into a vein (systemic chemo), directly into the cerebrospinal fluid (intrathecal chemo), or directly into the eye (intraocular chemo). Intraocular chemo gets higher doses of the drug to the tumor without causing severe side effects in other parts of the body. Methotrexate is the most commonly used chemo drug, but others can be used as well. [Monoclonal antibodies](#) such as rituximab may also be given directly into the eye. The best combination and dosage of drugs is not yet known, and the choice may be influenced by the type of lymphoma. Sometimes systemic chemo may be given along with therapy given directly to the eye such as external radiation or intraocular chemo.

If the lymphoma does not respond to treatment or if it comes back (recurs), [high-dose chemotherapy followed by a stem cell transplant](#) may be an option for some people.

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Treating T-Cell Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is generally divided into main 2 types, based on whether it starts in B lymphocytes (B cells) or T lymphocytes (T cells). There are many different types of T-cell lymphomas, and treatment can vary based on [which type you have](#)¹.

T-lymphoblastic lymphoma/leukemia

This disease can occur in both children and adults, and it can be considered either a lymphoma or a type of [acute lymphoblastic leukemia \(ALL\)](#)², depending on how much of the bone marrow is involved. (Leukemias have more bone marrow involvement.)

Regardless of whether it's labeled as a lymphoma or a leukemia, this is a fast-growing disease that's treated with intensive chemotherapy (chemo), when possible.

Combinations of many drugs are used. These can include cyclophosphamide, doxorubicin (Adriamycin), vincristine, L-asparaginase, methotrexate, prednisone, and, sometimes, cytarabine (ara-C). Because of the risk of spread to the brain and spinal cord, a chemo drug such as methotrexate is also given into the spinal fluid. Some doctors suggest maintenance chemo for up to 2 years after the initial treatment to reduce the risk of recurrence. High-dose chemo followed by a stem cell transplant may be another option.

Treatment is typically given in the hospital at first. During this time, patients are at risk for tumor lysis syndrome (described in [Chemotherapy for Non-Hodgkin Lymphoma](#)), so they are given plenty of fluids and drugs like allopurinol.

For more details on treatment, see [Treating Acute Lymphocytic Leukemia \(Adults\)](#)³ and

[Treating Childhood Leukemia⁴](#).

Although this lymphoma is fast-growing, if it hasn't spread to the bone marrow when it's first diagnosed, the chance of cure with chemo is quite good. But it is harder to cure once it has spread to the bone marrow.

Peripheral T-cell lymphomas

Cutaneous T-cell lymphomas (mycosis fungoides, Sezary syndrome, and others)

Treatment of these skin lymphomas is discussed in [Treating Lymphoma of the Skin⁵](#).

Adult T-cell leukemia/lymphoma

This lymphoma is linked to infection with the HTLV-1 virus. There are 4 subtypes, and treatment depends on which subtype you have.

- The **smoldering and chronic subtypes** grow slowly. Like other slow-growing lymphomas (such as follicular lymphoma and small lymphocytic lymphoma), these subtypes are often watched without treatment as long as they aren't causing problems other than mildly swollen lymph nodes. If treatment is needed, one option is interferon and the anti-viral drug zidovudine to fight the HTLV-1 infection. If the lymphoma is affecting the skin, it may be treated with radiation. Another option is chemo, using the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other combinations.
- The **acute subtype** also can be treated with either anti-viral drugs or chemo (typically the CHOP regimen). If it responds well to treatment, a stem cell transplant might be considered.
- Anti-viral therapy is not helpful for the **lymphoma subtype**, so it is typically treated with chemotherapy. It can also involve the tissues around the brain and spinal cord, so chemo is given into the spinal fluid (intrathecal chemo) as well. Treatment after chemo may include a stem cell transplant.

Because there is no clear standard treatment for this disease, patients might want to consider enrolling in a [clinical trial⁶](#), if one is available.

Angioimmunoblastic T-cell lymphoma

This fast-growing lymphoma might be treated first with steroids (such as prednisone or dexamethasone) alone, especially in older patients who might have trouble tolerating chemo. This treatment can reduce fever and weight loss, but the effect is often temporary. If [chemo](#) is needed, combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) may be used. Another option might be the chemo combination of cyclophosphamide, doxorubicin, and prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). If the lymphoma is only in one area, [radiation therapy](#) may be an option.

Standard doses of chemo rarely produce long-term remissions, so a [stem cell transplant](#) is often suggested after initial chemotherapy if a person can tolerate it.

Extranodal natural killer/T-cell lymphoma, nasal type

This rare lymphoma is often confined to the nasal passages. Patients with stage I or II disease who aren't healthy enough for chemotherapy may be treated with radiation therapy alone. Most other patients are treated with chemoradiation (chemo and radiation given together) or chemo followed by radiation. Several different chemo combinations can be used.

If the lymphoma doesn't go away completely, a stem cell transplant may be done if possible.

Enteropathy-associated T-cell lymphoma

This lymphoma generally develops in the small intestine or colon. Intensive chemo using several drugs is usually the main treatment. Often CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) is the chemo used. If the lymphoma is only in one area, radiation therapy may be used as well. But if these treatments work, a hole (perforation) can develop in the intestines (as the lymphoma cells die), so surgery might be done first to remove the part of the intestines containing the lymphoma. Surgery may also be needed before chemo or radiation if a person is diagnosed with this lymphoma because it caused a perforation or intestinal blockage (obstruction). A stem cell transplant may be an option if the lymphoma responds to chemo.

Anaplastic large cell lymphoma (ALCL)

This fast-growing lymphoma mainly affects lymph nodes and is treated with [chemo](#) regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone). Another option might be the chemo combination of cyclophosphamide, doxorubicin, and

prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). Doctors might recommend [radiation therapy](#) as well for some patients.

This lymphoma often responds well to treatment, and long-term survival is common, especially if the lymphoma cells have too much of the ALK protein. If the cells lack the ALK protein or if the lymphoma returns after initial treatment, a [stem cell transplant](#) may be an option. Another option for lymphomas that no longer respond to initial treatment is brentuximab vedotin (Adcetris).

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): For ALCL that develops in the capsule (normal protective scar tissue) that forms around a breast implant, experts typically recommend removing the implant and the capsule surrounding it. Additional treatment might include chemo, sometimes with radiation.

Peripheral T-cell lymphoma, unspecified

These lymphomas are generally treated the same way as diffuse large B-cell lymphoma (DLBCL). [Chemo](#) with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other drug combinations is used. For early-stage disease, [radiation therapy](#) may be added. Another option for some of these lymphomas might be the chemo combination of cyclophosphamide, doxorubicin, and prednisone, along with the [monoclonal antibody](#) brentuximab vedotin (Adcetris). A [stem cell transplant](#) may be recommended when possible.

If other treatments are no longer working, newer chemo drugs such as pralatrexate (Folotyn), [targeted drugs](#) such as bortezomib (Velcade) or belinostat (Beleodaq), or [immunotherapy](#) drugs such as alemtuzumab (Campath) and denileukin diftitox (Ontak) may be tried.

The outlook for these lymphomas is usually not as good as in DLBCL, so taking part in a [clinical trial](#)⁷ of newer treatments is often a good option.

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Treating HIV-Associated Lymphoma

People with [HIV infections](#)¹ are at increased risk for non-Hodgkin lymphoma. Although people with HIV tend to get more aggressive forms of lymphoma such as diffuse large B-cell lymphoma, primary CNS lymphoma, or Burkitt lymphoma, their outlook has improved a great deal in recent years. The use of highly active anti-retroviral therapy (HAART) to treat HIV has helped patients to better tolerate treatments such as chemo and immunotherapy.

A major problem in the past was that patients with HIV infection tended to have low blood cell counts to begin with, which made it hard to treat them with full doses of chemo. This problem has been relieved somewhat by the use of HAART and by the use of drugs to help the patient's body make new blood cells. Still, doctors give chemo cautiously and monitor blood counts closely. HIV can lower the number of white blood cells known as CD4-positive cells. People with low CD4 counts can have more problems when treated with rituximab, so some experts don't use this drug for patients who have low CD4 counts.

Most experts believe that the prognosis (outlook) for a person with HIV-associated lymphoma relates at least as much to the HIV infection as to the lymphoma. Modern anti-HIV therapy can often control the immune deficiency in patients with AIDS, so the outlook for patients who develop lymphoma has improved.

The treatment of the lymphoma itself depends on the specific type of lymphoma.

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