National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Primary Central Nervous System Lymphoma



Presented with support from NCCN FOUNDATION® Guiding Treatment. Changing Lives.

Available online at NCCN.org/patientguidelines



NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Central Nervous System Cancers, Version 2.2026 — June 10, 2026.

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1
About primary CNS lymphoma

5 What is primary CNS lymphoma?

7 How is primary CNS lymphoma diagnosed?

7 How is primary CNS lymphoma treated?

8 How can I get the best care?

Being diagnosed with a brain tumor is frightening and overwhelming. This guide will help you make sense of all the information out there. Ultimately, you'll have the knowledge to make confident decisions.

What is primary CNS lymphoma?

Primary central nervous system lymphoma is a rare and fast-growing cancer that affects the central nervous system (CNS). Cancer is what happens when cells grow out of control.

Let's break it down word by word to understand it better:

Primary – Primary means first. In cancer care, primary refers to the place where cancer first occurred. Primary CNS lymphoma occurs in the central nervous system.

Central nervous system – The CNS is made up mainly of the brain and spinal cord. Primary CNS lymphoma occurs more often in the brain than in the spinal cord, but it can also involve the cerebrospinal fluid and/or the eyes.

Lymphoma – Lymphoma is cancer that forms from lymphocytes. Lymphocytes are white blood cells that fight infections. Cancer is an abnormal overgrowth of cells. So, a lymphoma is an abnormal overgrowth of lymphocytes.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

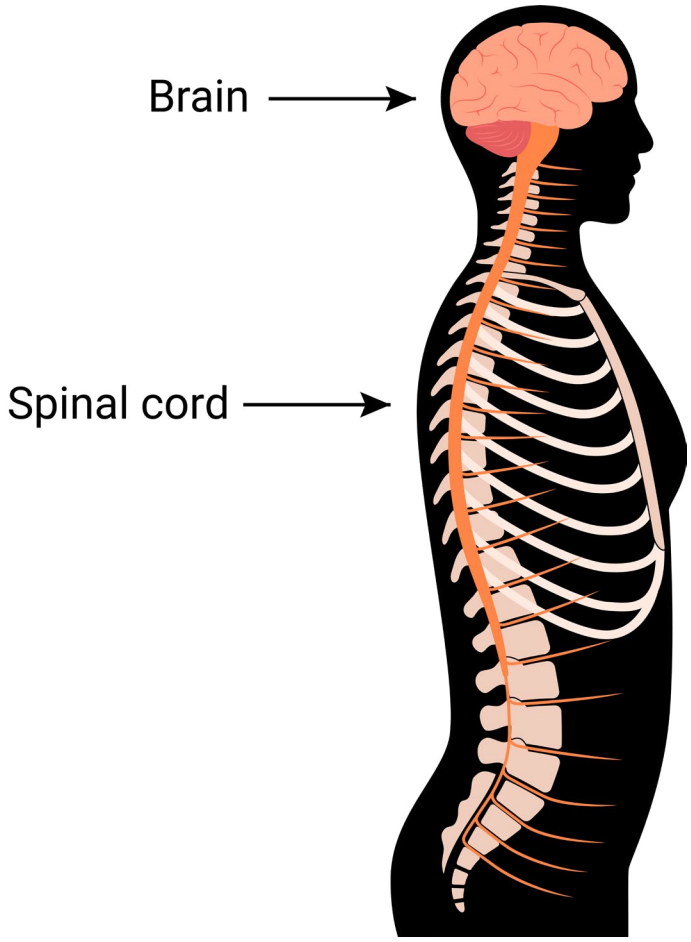
Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

Now let's put it all together:

Primary CNS lymphoma is a cancer that begins when lymphocytes in the brain and spinal cord grow out of control.

What is the CNS?



The central nervous system (CNS) receives signals from your senses, processes information, and controls your body's responses. Parts of the CNS include:

- **Brain**, which controls functions of the body, such as feeling, moving, thinking, and learning. The eyes are connected directly to the brain and are also part of the CNS.
- **Spinal cord**, which transmits messages between the brain and the body.
- **Meninges**, which are membranes that cover your brain and spinal cord.
- **Cerebrospinal fluid**, which is a liquid that surrounds your brain and spinal cord.

Bones protect the CNS. The skull shields your brain, and the vertebrae surround your spinal cord.

Primary CNS lymphoma starts from lymphocytes, which are part of the immune system. The immune system is your body's natural defense against infection and disease. Having an impaired immune system may increase the risk of developing this cancer.

Primary CNS lymphoma can spread to other areas within the nervous system. For example, it may spread from the brain to the eyes. But it rarely spreads outside of the CNS to other areas of the body.

How is primary CNS lymphoma diagnosed?

Primary CNS lymphoma is often found when a person develops symptoms. A symptom is a feeling or problem that may be a sign of disease. Primary CNS lymphoma can cause a variety of symptoms, which usually develop over several weeks.

Symptoms are often related to the cancer's location in the central nervous system. Primary CNS lymphoma is most commonly located in the brain. A lymphoma in the brain may cause specific nerve changes such as leg or arm weakness, or problems with coordination or movement.

Other symptoms may include changes in personality or behavior, depression, confusion, memory problems, loss of bladder control (incontinence), or difficulty speaking or swallowing.

As the lymphoma tumor grows, it puts pressure on the CNS. This pressure often leads to neurological symptoms and difficulties, including headaches, nausea, vomiting, or seizures. Changes in eyesight, such as blurry vision or double vision, can also occur.

You'll need several tests to confirm whether you have primary CNS lymphoma or a different disease with similar symptoms or characteristics. Important tests include a neurological exam, imaging (MRI or CT scan), and biopsies. A biopsy means taking a sample of fluids or tissue from your body to look for cancer. You'll also have blood tests, an eye exam, and other tests.

If these tests show that you have primary CNS lymphoma, your doctor and care team should discuss your treatment options with you. If possible, seek care at a center with experience in treating lymphomas in the brain.

How is primary CNS lymphoma treated?

The main treatments for primary CNS lymphoma include chemotherapy, radiation therapy, stem cell transplant, or a combination of these treatments. Joining a clinical trial of a potential new therapy is another recommended option.

Treatment for primary CNS lymphoma can slow its growth, reduce your symptoms for a period of time, and prolong your life.

Treatment may be able to put primary CNS lymphoma into remission. Remission means there are no symptoms or signs of cancer. Remission may last for months or years. However, even with the best treatment, primary CNS lymphoma often comes back (relapses) in the brain, spinal cord, or the eye.

It's true that primary CNS lymphoma is fatal for some patients. Still, there's hope. In the past few years, improved detection methods have shortened the time to diagnosis and led to better outcomes, including for people with weakened immune systems.

Therapies specifically designed to treat primary CNS lymphoma are currently being studied in clinical trials. The number of these trials has increased in recent years, offering more hope to people living with this disease.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

A message to caregivers and loved ones

This guide is for you, too. This guide will help you understand this disease and the challenges it presents.

People with lymphoma in the central nervous system (the brain and spinal cord) commonly develop problems with brain function. This can show itself in multiple ways, such as slower thinking, memory loss, difficulty moving or walking, trouble speaking, inability to do everyday activities, changes in behavior, losing one's sense of self, and other problems.

Helping a person with primary CNS lymphoma can be challenging and time-consuming. You may be providing physical, mental, emotional, and hands-on support. You may be taking the patient to appointments, helping to lessen side effects, and even assisting with treatment decisions.

Gather as much help as you can. Start with the online resources listed in the back of this guide.

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Testing for primary CNS lymphoma

10 Tests for diagnosis

14 Tests after diagnosis

18 Key points

19 Questions to ask

Different tests are needed to identify primary central nervous system (CNS) lymphoma and to make a treatment plan. The key to confirming the diagnosis is removing a small sample of the tumor tissue and testing it for lymphoma cells.

Tests for diagnosis

Many diseases have signs and symptoms similar to primary central nervous system (CNS) lymphoma, including neurological illnesses and other types of brain cancer. But primary CNS lymphoma is treated differently from lymphomas in other parts of the body. So it's important to have tests to confirm your diagnosis. See **Guide 1**.

If you're diagnosed with primary CNS lymphoma, you'll have additional tests to find out how far the cancer extends within the central nervous system.

Guide 1
Tests to diagnose primary CNS lymphoma and to make your treatment plan

Neurological exam	
Imaging scan of the brain	• MRI • CT scan if needed
Imaging scan of the spine if needed	• MRI
Imaging of whole body or upper body if needed	• PET/CT • CT
Eye exam	
Blood tests	• Lactate dehydrogenase test • HIV test if needed • Hepatitis B test if needed
Biopsy	• Biopsy of the brain tumor (stereotactic biopsy) • Biopsy of the eye if needed • Biopsy of the spinal fluid (lumbar puncture) if needed • Biopsy of the bone marrow if needed

Tests are also used to help plan your treatment.

If you haven't yet been diagnosed with primary CNS lymphoma, you'll first have a physical examination and some general health assessments. These include a neurological exam and an evaluation of your level of activity. After these, you'll have imaging scans and 1 or more biopsies.

Neurological exam

This exam involves some simple tests to check your alertness, balance, coordination, reflexes, hearing, and other senses. Your doctor or a specialist may also perform an eye exam to look at the health of the nerves in the back of your eye.

Imaging

Imaging tests take pictures (images) of the inside of your body. The images show areas in the body that might have cancer. The images can reveal a lymphoma's location, size, and other features.

Although many people with primary CNS lymphoma have only 1 visible tumor, others have multiple tumors on their scan.

You may need more than 1 type of scan for the same part of the body because different scans provide different types of information to guide treatment.

MRI

MRI is the most useful imaging technique for identifying primary CNS lymphoma. MRI scans are good at showing the spine and soft tissues, including the brain, as well as other details that are helpful for planning surgery.

During an MRI, you'll lie on a table that slides into the scanning machine. MRI uses radio waves and magnets to take pictures of the inside of your body. It doesn't use radiation like x-rays or CT scans.

MRI of the brain

Magnetic resonance imaging (MRI) is the most useful imaging technique for identifying primary CNS lymphoma.

It's important to lie still during the test to get the best images. Straps or other devices may help you avoid moving.



An MRI of the brain or spinal cord usually requires a contrast agent (also called contrast dye, or just contrast). Contrast highlights areas in organs, blood vessels, or other tissues to make them easier to see.

Contrast is injected into the bloodstream through an intravenous (IV) line before or during the imaging test and is later flushed out in urine. The contrast agent used for primary CNS lymphoma is called gadolinium.

You'll have multiple MRI tests throughout diagnosis and treatment. An MRI should be done early on if your symptoms suggest a brain tumor. It's also used right after treatment to see how well the treatment worked.

You'll have more MRIs during follow-up to watch for any recurrence or new growth.

CT

If MRI is unavailable or not recommended for you, you might have a computed tomography (CT or CAT) scan instead.

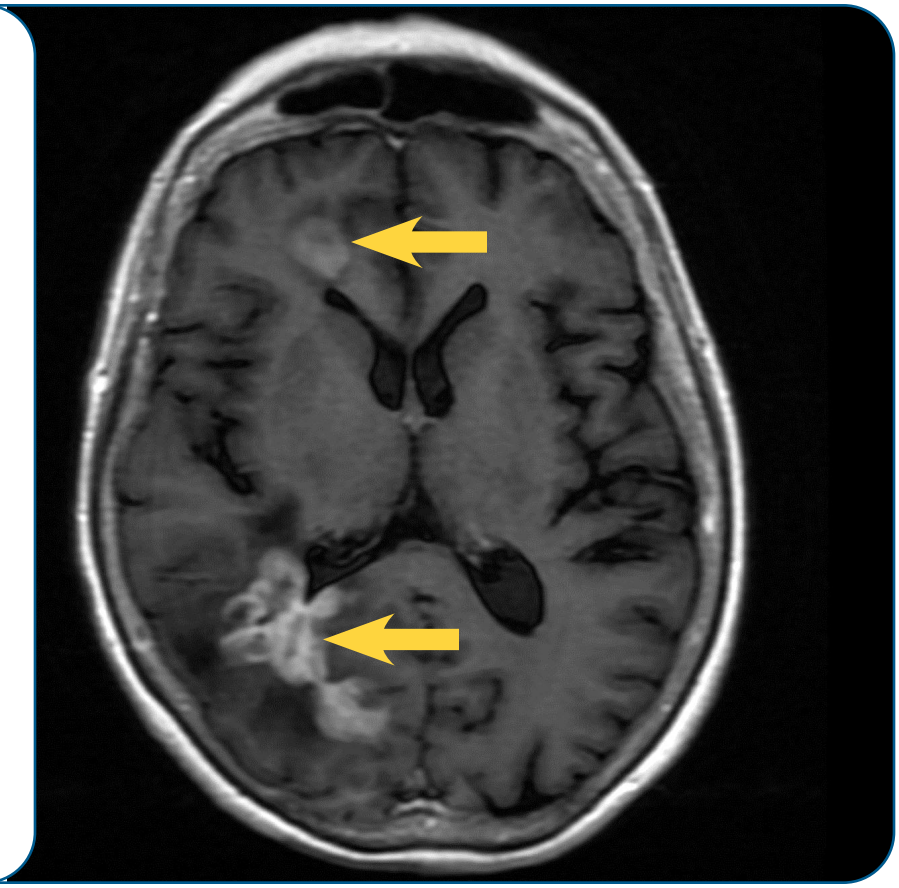
A CT scan uses x-rays to take many images from different angles. A computer then combines the pictures to make a series of cross-sectional images of your body.

What an MRI shows

This MRI scan highlights primary CNS lymphoma in the brain.

People with primary CNS lymphoma may have only 1 tumor or multiple tumors on their scan.

Image: Stephanie E. Weiss, MD, FASTRO



After imaging

After the MRI or CT scan, your images will be studied by a radiologist, an expert in analyzing images of the nervous system.

The radiologist will convey the imaging results to your doctor and care team. This information helps your team plan what the next steps of your care should be.

If your imaging results suggest primary CNS lymphoma, the next step is usually a biopsy.

Biopsy

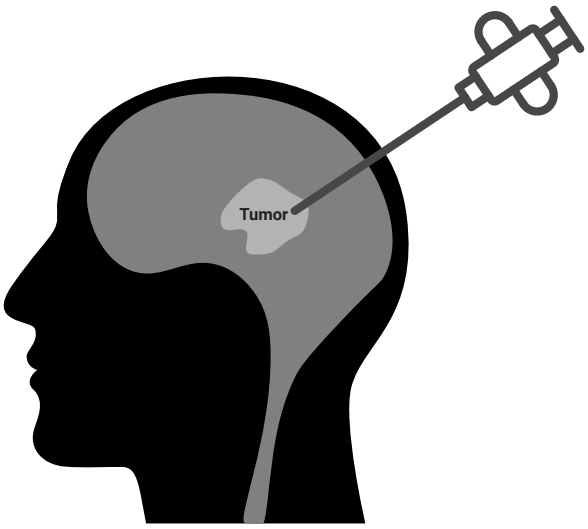
If imaging scans show something that could be a primary CNS lymphoma, your care providers will want to take a sample and test it.

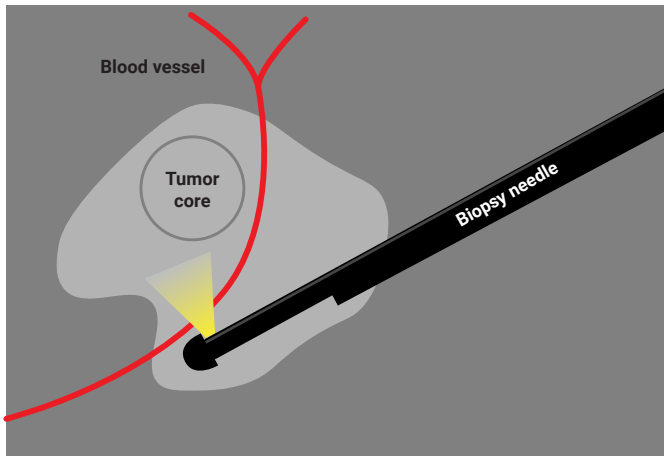
A biopsy is a procedure that removes a small piece of tissue for testing. Getting a biopsy is the main way to be certain that you have cancer and to find out what kind it is. A biopsy also gives your care team clues about how to treat it.

In some cases, a spinal tap to sample the spinal fluid can make the diagnosis without a biopsy.

Stereotactic biopsy

A stereotactic biopsy is needed to diagnose primary CNS lymphoma. In this procedure, a thin, hollow needle is inserted into the brain to remove a sliver of the tumor. The sample is sent to a lab to be tested for cancer cells.





Stereotactic biopsy

The standard method for diagnosing primary CNS lymphoma is a stereotactic biopsy. It's the recommended procedure when a brain tumor is in a hard-to-reach or vital area. It aims to remove only enough of the tumor to make a diagnosis.

A stereotactic biopsy is done by a neurosurgeon in an operating room.

First, you'll be fitted with a frame or several tiny markers around your head to aid the surgery. Next, you'll be given anesthesia to go to sleep. A small area of your hair will be shaved.

The neurosurgeon will then make a little opening in your skull and insert a thin, hollow needle into the brain to remove a sliver of the tumor.

A computerized navigation system, connected to MRI or CT imaging, will allow the surgeon to target and remove the sample with a high degree of precision.

After removal, the opening in your scalp will be closed with sutures. Many people go home the same day or the next day.

Meanwhile, the tissue sample is sent to a laboratory for analysis. A specialist called a pathologist will examine the tissue under a microscope.

If the tissue is cancerous, the pathologist will identify the type and grade of the cancer. The testing process takes about 1 or 2 weeks to complete.

If stereotactic biopsy is unavailable at your hospital or medical center, ask to be referred to a specialized center where it can be done.

Tests after diagnosis

After an MRI scan and a stereotactic biopsy have confirmed a diagnosis of lymphoma in the central nervous system, a few more tests are needed to find out which area or areas of the CNS are affected with tumor cells.

Testing after diagnosis also checks for signs of cancer in the eyes, cerebrospinal fluid, blood, chest, abdomen, and pelvis, and possibly the bone marrow or testicles. These tests include an eye exam, a spinal tap, more imaging, various blood tests, and possibly a bone marrow biopsy.

"Don't Google your diagnosis [or run it through AI] and assume that statistics define your life! Every person's brain tumor story and situation is different. My motto is to 'live fearlessly' and ignore those fears the internet can give you."

Eye exam

Your eyes are connected directly to your brain. Lymphoma rarely occurs in the eyes. But if it does, it usually develops in the back of the eye, which is called the retina. The retina converts what you see into signals, which it sends through the optic nerves to the brain.

Lymphoma cells can also invade the vitreous, the clear gel that fills the eye. When primary CNS lymphoma involves the eyes, it's called vitreoretinal lymphoma.

Everyone diagnosed with primary CNS lymphoma should have a thorough eye exam. This is done at an eye doctor's office using a slit lamp, which is a microscope with a bright light.

You'll be given drops in your eyes to widen (dilate) your pupils. This gives the eye doctor a better view inside your eyes. The doctor then uses the bright light to examine your retina, optic nerve, and other parts of your eyes.

Biopsy of the eye

If the vitreous looks unusual or you have visual symptoms, you may need a biopsy of the vitreous.

For this procedure (called a vitrectomy), your eye is first numbed with anesthetic. Then a thin needle is inserted into the eye. The needle removes a tiny amount of vitreous, which is then tested for cancer cells.

In some cases, a vitrectomy alone can confirm the diagnosis of primary CNS lymphoma without the need for a brain biopsy.

CNS lymphoma in the eye

Primary CNS lymphoma can occur in the brain, the spinal cord, and sometimes in the eyes. Everyone diagnosed with primary CNS lymphoma should have a thorough eye examination.

Here, an ophthalmologist uses a special microscope called a slit lamp to take a close-up look at a patient's eye.



Spinal tap

A spinal tap (also called a lumbar puncture) is a procedure that removes a small amount of cerebrospinal fluid (CSF) for testing. CSF flows in and around the hollow areas in the brain and spinal cord. This fluid protects and nourishes the central nervous system.

If a stereotactic biopsy isn't possible, testing the CSF can help confirm a diagnosis of primary CNS lymphoma. Testing also provides other helpful information needed for planning treatment.

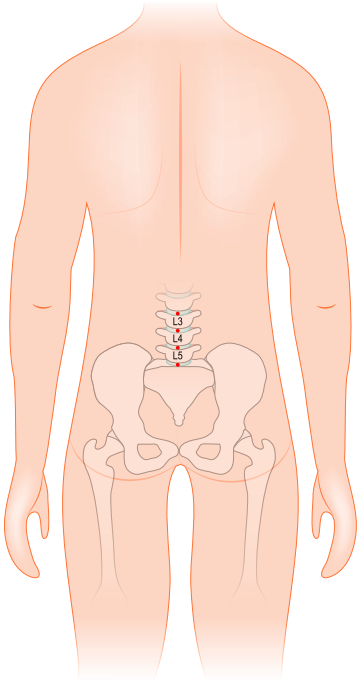
A spinal tap is done only if it can be performed safely and won't delay treatment.

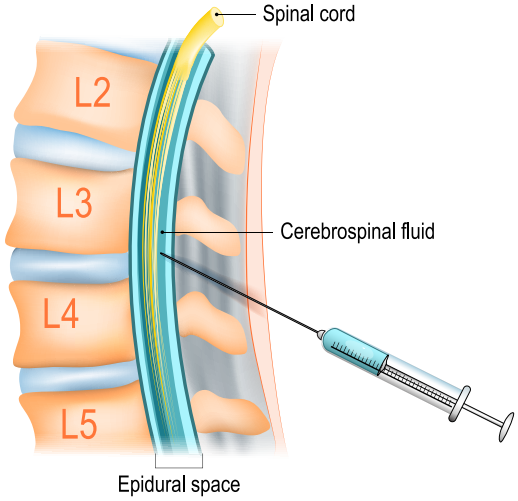
If cancer cells are found in the spinal fluid, or you're having symptoms, another MRI may be needed to find out if there are any lesions in the spine.

Spinal tap

Cancer cells in the spinal fluid may or may not cause symptoms. A spinal tap (also called a lumbar puncture) is used to learn whether cancer has spread to the spinal cord.

First, the lower back is numbed. Then a long, thin needle is inserted into the lower part of the spinal column to remove cerebrospinal fluid. The fluid is then sent to a lab for testing.





More imaging

It's uncommon for primary CNS lymphoma to spread outside of the CNS or the eyes. Still, it's important to examine the rest of your body just to be sure.

The imaging methods most commonly used for this are positron emission tomography (PET) and/or computed tomography (CT).

- **PET imaging** uses a small amount of a radioactive substance to find cancer cells in the body. After the radioactive drug is injected into a vein, it causes cancer cells to show up as bright spots on PET scans.
- **CT scan** of the chest, abdomen, and pelvis is recommended to look for cancer that has spread to these areas. A contrast agent is injected into the bloodstream before the scan to make the areas of cancer easier to see.
- **PET/CT** scan combines PET imaging with CT to get a clearer picture of where the lymphoma cells are most active throughout the whole body.

Blood tests

Blood tests can also help establish the extent of the cancer and provide other information needed for planning your treatment. In addition to standard blood tests, other recommended blood tests include:

- **Lactate dehydrogenase (LDH)** is an enzyme involved in converting food into energy for the body. An LDH test measures this enzyme in your blood. A high level of LDH can be a sign of cell damage caused by cancer or other health problems.
- **Human immunodeficiency virus (HIV) blood test** is needed for everyone with primary CNS lymphoma. HIV related to primary CNS lymphoma requires specialized care and treatment with antiretroviral therapy in addition to cancer treatment.
- **Hepatitis B testing** is necessary if you're having immunotherapy treatment and you've had this virus before (or you're at risk of getting it). Immunotherapy can reawaken the hepatitis B virus and cause illness that interferes with treatment.

Bone marrow biopsy

Most bones have a spongy center called marrow, where new blood cells are made.

It's uncommon to find lymphoma cells in the bone marrow of people diagnosed with primary CNS lymphoma. But if imaging suggests the possibility of lymphoma in the bones, a biopsy of the bone marrow may be recommended.

In this procedure, a hollow needle is inserted into the bone (usually at the back of the hip bone), and a sample of marrow is removed. The marrow sample is then sent to a lab for testing.

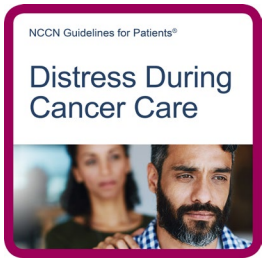
Key points

- A biopsy is the main test to diagnose primary central nervous system (CNS) lymphoma.
- A biopsy is a procedure that removes a small piece of a tumor, which is tested for cancer cells.
- The standard biopsy method for diagnosing primary CNS lymphoma is a stereotactic biopsy.
- A stereotactic biopsy is a precise technique that's used when a brain tumor is in a hard-to-reach or vital area.
- After primary CNS lymphoma is diagnosed, more tests are needed to find out which area of the CNS is affected with tumor cells.
- Everyone diagnosed with primary CNS lymphoma should have a thorough eye examination to look for lymphoma in the eyes.
- A spinal tap (lumbar puncture) is a procedure that removes a small amount of cerebrospinal fluid, which is tested for cancer cells.

Don't dismiss your distress

Depression, anxiety, and distress are very common in people with cancer (and their caregivers, too).

- About 1 in 3 patients with primary brain tumors develop clinical depression and anxiety at some point.
- Up to 3 out of 4 people with primary brain tumors experience psychological distress.



Tell your treatment team if you're feeling stressed or overwhelmed. Ask them for help. You don't have to cope with it by yourself.

Read more about cancer and distress in *NCCN Guidelines for Patients: Distress During Cancer Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Questions to ask

- What tests will I have?
- Where do I go for testing, and how long will it take?
- Do I need to do anything to prepare for testing?
- Do the tests have any risks?
- How soon will I know the results and who will explain them to me?

What's next?

After you've been diagnosed and have gone through further testing to find out the extent of the lymphoma, your treatment team will discuss your results with you. You'll also talk about your choices for treatment. The next chapter explains the different options for treating primary CNS lymphoma.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer. Take our survey to let us know what we got right and what we could do better.
NCCN.org/patients/feedback

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Types of treatment

21 Clinical trials

23 Steroids

23 Chemotherapy

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31 Questions to ask

This chapter lists the different treatment options for primary central nervous system (CNS) lymphoma. Ask your doctor about the risks and benefits of each option. Together, you and your team can make a treatment plan.

There's no single drug or procedure that's best for treating primary central nervous system (CNS) lymphoma. The best treatment is the one that works best for you.

Treatment options include corticosteroids, chemotherapy, radiation therapy, targeted therapy, immunotherapy, stem cell transplant, and in certain cases CAR T-cell therapy. Receiving treatment in a clinical trial is also a recommended option.

Therapies are often combined to treat lymphoma. For example, chemotherapy may be given with an immunotherapy drug, or several chemotherapy drugs may be given together. Chemotherapy is also an essential part of having a stem cell transplant.

Surgery is not normally an option. Because primary CNS lymphoma usually develops deep within the brain tissue, removing it with surgery is risky and may be more harmful than helpful.

Treatment is usually given in phases (which are discussed in the next chapter).

Clinical trials

NCCN experts recommend that everyone with primary CNS lymphoma consider joining a clinical trial for treatment.

A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of fighting cancer need to be studied in people.

If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. FDA.

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

Phases

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

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

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

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

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

Worldwide

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

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

NCCN experts recommend that everyone with primary CNS lymphoma consider trying to join a clinical trial for treatment.

Ask about clinical trials available to you and the services your hospital and other facilities provide to cancer patients, such as counseling, nutritional advice, meditation, physical therapy, palliative care, and integrative medicine. Don't be shy. Be your own advocate—or ask someone close to be one for you."

Steroids

Corticosteroids (often just called steroids) are common medications that shrink inflammation and control swelling. Steroids are used to shrink primary CNS lymphomas and decrease swelling in the brain. This can rapidly reduce the signs and symptoms of the lymphoma.

However, steroids lose their effectiveness and cause side effects when you take them long-term. So steroids are only given for a short period of time, usually in newly diagnosed patients.

If possible, steroid therapy should be delayed until you have a biopsy and get a diagnosis. This is because steroids can change the appearance of lymphoma cells, making it difficult to reliably diagnose the disease.

Side effects of steroids

Common side effects of steroids are feeling hungry, trouble sleeping, slow wound healing, upset stomach, mood changes, and swelling in the ankles, feet, and hands. Steroids may also significantly increase blood sugar levels and weaken your immune system.

Most side effects of steroids go away after the drug is stopped.

Chemotherapy

Chemotherapy is drug treatment that damages and destroys rapidly dividing cells throughout the body. Because cancer cells divide and multiply rapidly, they're a good target for chemotherapy.

But chemotherapy harms healthy cells, too. Damage to healthy cells can cause side effects.

Treatment for primary CNS lymphoma may include a single chemotherapy drug or a combination of drugs. A combination is sometimes chosen because the drugs work better when they're used together.

The most common chemotherapy used for primary CNS lymphoma is methotrexate given in high doses and combined with other chemotherapies or drugs.

Methotrexate and most other chemotherapy drugs for primary CNS lymphoma are given intravenously (IV). This means the medicine is slowly infused through a tube into a vein in your arm or another part of your body. The medicine travels in the bloodstream to reach cells throughout your body.

Some chemotherapy drugs can be taken by mouth as a tablet or capsule.

Chemotherapy is given in cycles. One cycle involves a few days of treatment followed by several days of rest. Different chemotherapy drugs have different cycles. Common cycles are 14, 21, or 28 days. Having chemotherapy in cycles gives your body a chance to recover after treatment.

Intrathecal chemotherapy

If lymphoma cells are found in the cerebrospinal fluid (CSF) or if an MRI of the spine shows cancer, chemotherapy may be infused directly into the CSF in some cases. This is known as intrathecal or intra-CSF chemotherapy.

Intrathecal chemotherapy is used only in select cases of lymphoma in the spine or CSF, or as part of a specific treatment program for primary CNS lymphoma.

Intraocular chemotherapy

In rare cases, primary CNS lymphoma occurs in the eye. An ophthalmologist (an eye specialist) or another specialist may perform the examination or provide treatment. In these situations, chemotherapy may be infused into a vein or directly into the eye.

Possible side effects from intraocular chemotherapy include eye irritation, infection, inflammation, and cataracts. Cataracts can be treated with a routine operation by an eye surgeon.

Side effects of chemotherapy

Like other therapies, the side effects of chemotherapy depend on many factors. These include the drug, the dose, and the person.

Chemotherapy, especially in high doses, may not be the right treatment for people who are frail or older. These individuals may have a difficult time dealing with the harsh side effects.

When methotrexate is given in high doses, for instance, it may cause damage to the kidneys, liver, and other organs. In severe cases, kidney failure is possible.

To reduce this risk, you'll need to stay at the hospital during methotrexate treatment and receive fluids through a vein in your arm.

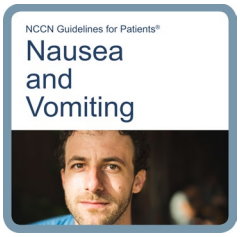
You may also be given leucovorin as part of your treatment. Leucovorin is a medicine that reduces the harm of methotrexate in your body and prevents severe problems in your kidneys and other organs.

Many cancer treatments, including chemotherapy, can lead to birth defects. So avoid becoming pregnant or getting someone pregnant while on chemotherapy treatment.

Other side effects of chemotherapy include nausea, vomiting, diarrhea, mouth sores, loss of appetite, hair loss, low blood cell counts, and feeling very tired or weak (fatigue). Other side effects are also possible.

Medicines are available during chemotherapy treatment to help control most of these side effects.

More information on nausea and vomiting can be found in *NCCN Guidelines for Patients: Nausea and Vomiting*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Radiation therapy

Before effective chemotherapy became available to treat primary CNS lymphoma, radiation therapy was the most commonly used treatment. It's still an option for treating primary CNS lymphoma in people who can't have chemotherapy in the first phase of treatment (induction).

Radiation is sometimes used is in the second phase of treatment (consolidation) to kill cancer cells left over after the first phase of treatment.

Radiation therapy uses high-energy x-rays or other radiation to kill cancer cells. Like x-rays used for imaging, you won't see or feel anything during treatment.

The total amount of radiation is usually divided into small doses given over several weeks. Smaller doses of radiation, given every day, damage the tumor while better preserving the healthy tissue.

What about side effects?

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Every treatment for primary CNS lymphoma can cause side effects.

Side effects depend on many factors, such as the drug, the amount taken, the length of treatment, and the person. Each person has an individual response to a drug. Some people have many side effects. Others have few.

Some side effects can be very serious. Others are not serious but are still unpleasant. Most side effects appear shortly after treatment starts and stop after treatment. Other side effects are long-term or may even appear years later.

Your treatment team will monitor your side effects during and after your treatment. Ask your team for a complete list of common and rare side effects of each treatment.

If a side effect bothers you, tell your treatment team. Often there are ways to prevent or avoid some side effects and help you feel better.

Whole-brain radiation therapy

The most commonly used radiation technique for primary CNS lymphoma is treatment of the entire brain, called whole-brain radiation therapy (WBRT). Because primary CNS lymphoma can occur in multiple spots anywhere in the brain, WBRT is used to treat the entire brain all at once.

WBRT can reach the upper part of the spine and some or all of the eyes. WBRT even treats microscopic tumors in the CNS that aren't visible on an MRI scan.

You'll need to remain as motionless as possible during each scan. You may be fitted with something that looks like a hockey mask, which will help keep you in position for treatment.

Radiation therapy for the eyes

Radiation therapy is also used to treat primary CNS lymphoma in the eyes. Radiation to the brain can be enlarged to include the eyes. Or radiation can be focused only on the eyes but at a lower dose. With either method, usually both eyes are treated at the same time.

Possible side effects include vision problems that may be temporary or permanent. Radiation therapy may cause cataracts, which can be treated with a routine cataract surgery.

Side effects of radiation therapy

Your radiation oncologist will discuss the possible side effects of WBRT. Side effects differ from person to person.

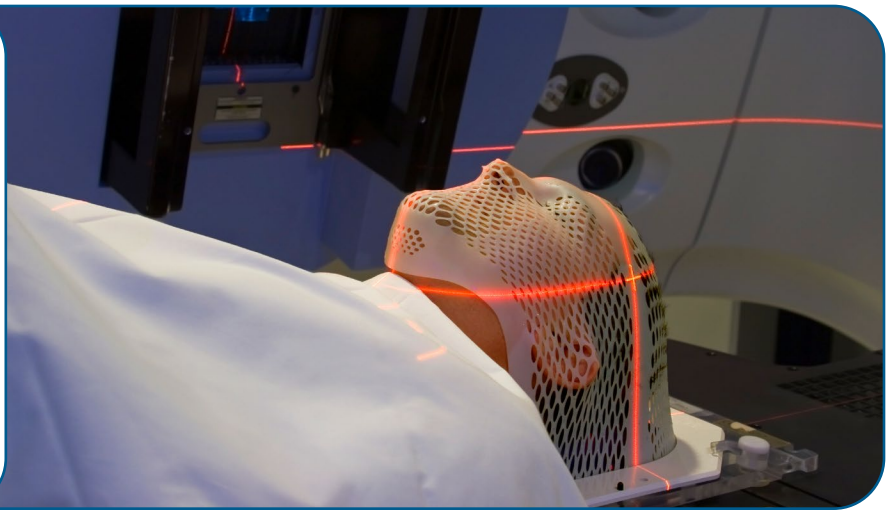
Common side effects include headaches, nausea, vomiting, and loss of appetite. These can be controlled by steroids or other medications during treatment.

Fatigue may begin during or after the treatment has finished and can last for several weeks.

Radiation therapy may be more likely than chemotherapy to have long-term side effects, especially in older adults. Months or years after WBRT, patients may develop memory problems, slowed thinking, or difficulty multitasking. Some people have trouble speaking.

Radiation therapy

Radiation therapy sends beams of intense energy to kill cancer cells. You'll need to remain as motionless as possible during each scan. You may be fitted with a mask or supports to help you lie still.



Fine motor skills, such as handwriting or tying shoes, may also be affected.

Talk to your doctor and treatment team about the benefits of radiation therapy compared with the risk of nervous system damage, including long-term problems with cognition.

Targeted therapy

Targeted therapy is another treatment for primary CNS lymphoma that can be combined with chemotherapy. Targeted therapy drugs attack specific parts of cancer cells to kill these cells or to slow their growth and spread.

Targeted therapies for some people with primary CNS lymphoma are medicines that block specific signals lymphoma cells use to grow. These include:

- BTK inhibitors such as ibrutinib (Imbruvica) and, in certain cases, zanubrutinib (Brukinsa)
- Immunomodulatory drugs such as lenalidomide (Revlimid) and pomalidomide (Pomalyst)

Side effects of targeted therapy

Some common side effects of targeted therapy include allergic reactions, fever, chills, muscle aches, fatigue, weakness, infections, nausea, and diarrhea.

Medicines are available during treatment to help reduce most of these side effects.

Immunotherapy

Immunotherapy uses your body's immune system—your natural defense against infection and disease—to fight cancer. Immunotherapy treats cancer cells throughout the body.

The main immunotherapy drug used for primary CNS lymphoma is rituximab (Rituxan). Rituximab is a type of immunotherapy called a monoclonal antibody.

Monoclonal antibodies hunt for specific proteins on the surface of cancer cells. Cancerous blood cells (and some healthy blood cells) have a protein on their surface called CD20. Rituximab finds and attaches itself to CD20 proteins. This helps your immune system locate and then destroy the cancer cells.

Rituximab is given through an IV infusion.

Side effects of immunotherapy

Rituximab and other immunotherapies may cause drowsiness, fatigue, constipation, joint pain, loss of appetite, low blood cell counts, and serious blood clots.

These medicines can also cause reactions related to the infusion itself, such as fever, chills, rash, swollen lips or tongue, dizziness, shortness of breath, or trouble breathing. Get medical help right away if you have any infusion-related reaction.

Stem cell transplant

A stem cell is a basic cell that can develop into any kind of cell. Stem cells that become blood cells are called hematopoietic cells. Hematopoietic means blood-forming. Blood-forming stem cells are made in the bone marrow.

But cancer and its treatment can damage and destroy cells in the bone marrow. When hematopoietic stem cells are damaged, they may not be able to make all the blood cells that the body needs.

A stem cell transplant (sometimes called a stem cell rescue) is a way to jump-start the bone marrow to make more healthy blood cells.

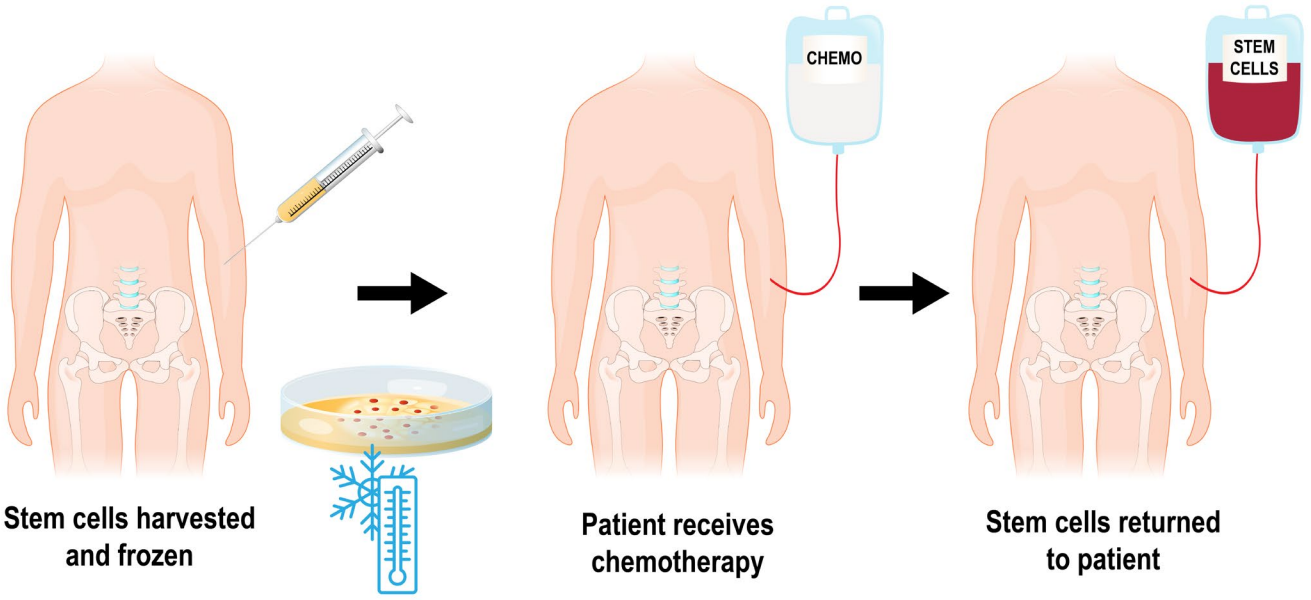
The process uses your own blood-forming stem cells to regrow your bone marrow.

High-dose chemotherapy and stem cell transplant

First, stem cells are removed (harvested) from your blood or bone marrow. The harvested stem cells are concentrated and frozen for preservation.

Next, you'll have high-dose chemotherapy to destroy any cancer cells in your body. This also kills all the stem cells in the bone marrow.

Lastly, the harvested stem cells are returned (transfused) to your body, where they'll grow new, healthy, blood-forming stem cells in the bone marrow.



A stem cell transplant has 3 key steps:

- **Stem cell removal** – First, some of your healthy stem cells will be removed from your blood or bone marrow. You may need a few visits to collect enough stem cells. The collected cells are frozen and stored for later.
- **High-dose chemotherapy** – Next, you'll receive intensive chemotherapy to kill any lymphoma cells in your body. The chemotherapy also kills all the stem cells in your bone marrow. Because your blood count will be low, your body will be very vulnerable to infections at this time, and you'll feel very fatigued.
- **Stem cell replacement** – After chemotherapy, your healthy stem cells will be thawed and returned to your body to "rescue" your damaged bone marrow. Your transplanted stem cells will migrate to the bone marrow and start to grow new blood stem cells. This will also begin to restore your body's ability to protect itself from infection.

You'll grow back blood cells and bone marrow in a few weeks, but it may take a year for your body to fully recover.

During this time, you'll have frequent blood tests and health checkups until your bone marrow is restored and your blood cell counts return to normal.

A stem cell transplant can be an intense procedure. It's not for everyone with primary CNS lymphoma. And it's only used after you've had other treatments or if the lymphoma comes back after earlier treatment (relapse).

Quality of life

Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities. Quality of life should be the main priority that guides your treatment and care.

Successful treatment isn't just about reducing the cancer. Other goals include minimizing cognitive problems, reducing pain, lowering anxiety and stress, carrying out regular activities, being with friends and family, and enjoying life as best as you can.

Your treatment team will consider many factors to decide if a stem cell transplant is right for you. Some of these factors include your fitness level, health status, organ function, cancer stage, previous treatments, other medical conditions, available supportive care, and additional factors, including your goals and preferences.

Because the procedure can be risky and the side effects harsh, a stem cell transplant may not be a useful option for people who are older or frail. Ask your team about the benefits and risks of having a stem cell transplant.

Side effects of stem cell transplant

Most side effects of a stem cell transplant come from the chemotherapy. High-dose chemotherapy can result in nausea, vomiting, diarrhea, hair loss, mouth sores, and other side effects.

Medicines are available during chemotherapy to help reduce most of these side effects.

You'll also likely feel tired and weak after the procedure and while waiting for the new blood stem cells to grow in the bone marrow. This should get better over time as you recover.

Supportive care

Supportive care (also called palliative care) is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. Although end-of-life care is a part of supportive care, supportive care is much more than that.

Supportive care is an important part of high-quality, comprehensive cancer care. Its goal is to control symptoms, relieve emotional and physical suffering that comes from the diagnosis and treatment of cancer, and improve the quality of life for people with cancer and their loved ones and/or caregivers.

For more about supportive care, turn to *Chapter 5: Follow-up care and further treatment*.

Your multidisciplinary team

When all of your doctors, specialists, nurses, and allied health providers are working and communicating as a team to help you, it's called multidisciplinary care.

Be clear about your treatment goals when you talk with your multidisciplinary team.



Key points

- A recommended treatment option for primary central nervous system (CNS) lymphoma is participating in a clinical trial.
- Other treatment options include corticosteroids, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and stem cell transplant. Often, some of these therapies are combined to treat primary CNS lymphoma.
- Chemotherapy is a drug treatment that damages and destroys rapidly dividing cells throughout the body. The main chemotherapy drug used to treat primary CNS lymphoma is methotrexate.
- Whole-brain radiation therapy (WBRT) is the most commonly used radiation technique for primary CNS lymphoma.
- Targeted therapy drugs attack specific parts of cancer cells to slow their growth and spread.
- Immunotherapy uses your body's immune system to fight cancer. The main immunotherapy drug for primary CNS lymphoma is rituximab.
- Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities.

Questions to ask

- What are the most appropriate treatment options for my situation?
- Will any of these treatments hurt or cause a lot of side effects?
- Are you suggesting treatment options from the NCCN Guidelines, or have you modified the standard approach for my situation?
- How do I get a second opinion?

What's next?

The next chapter explains the phases of treatment and what your individual treatment plan may be.

4
Phases of treatment

33 First phase of treatment

35 Second phase of treatment

37 Treatment for the spine

38 Treatment for the eyes

38 Key points

39 Questions to ask

Treatment for primary central nervous system (CNS) lymphoma should start soon after diagnosis. This chapter describes what to expect from the treatment process and explains the options for each phase of treatment.

Although there are different treatment options for primary central nervous system (CNS) lymphoma, the treatment approach is often a 2-step process.

The first step (called the **induction phase**) aims to destroy as many lymphoma cells as possible.

The goal of the second step (called the **consolidation phase**) is to destroy any cancer cells that may remain in the body after the first phase. Consolidation treatment also aims to prevent the lymphoma from returning.

First phase of treatment

The first (induction) phase of treatment can last several months. Treatment typically requires multiple courses of chemotherapy, which are given while you're in the hospital. The options for induction treatment are listed in **Guide 2** and discussed here.

Guide 2
First-phase (induction) treatment for primary CNS lymphoma

Type of treatment	Drugs used in the treatment
Treatment in a clinical trial	Depends on the individual trial
High-dose chemotherapy + immunotherapy	High-dose Methotrexate plus Rituximab
	High-dose Methotrexate, Leucovorin, and Temozolomide, plus Rituximab
	High-dose Methotrexate, Leucovorin, Cytarabine, and Thiotepa, plus Rituximab
High-dose chemotherapy + immunotherapy, and possibly whole-brain radiation therapy	High-dose Methotrexate, Leucovorin, Procarbazine, and Vincristine, plus Rituximab
	High-dose Methotrexate, Leucovorin, and Temozolomide, plus Rituximab

Clinical trial

Everyone with primary CNS lymphoma is encouraged to consider enrolling in a clinical trial. Joining a clinical trial allows you to receive treatment while also helping researchers learn more about this uncommon cancer.

The treatment you receive in the trial may or may not work better than the standard treatments for primary CNS lymphoma. Ask your care team if there is a clinical trial you may be eligible for.

High-dose chemotherapy

If you don't want to join a clinical trial or none are available for you, the recommended induction treatment is high-dose methotrexate chemotherapy, often given with other chemotherapies.

Methotrexate is the most effective chemotherapy drug for primary CNS lymphoma. Methotrexate has been used for many years to treat a variety of lymphomas and cancers.

Methotrexate works by blocking the body's use of folate, a form of vitamin B. Lymphoma cells can't multiply and spread as quickly without folate.

High doses of methotrexate are needed to break through the blood-brain barrier and still have enough strength to kill lymphoma cells. The blood-brain barrier is a protective layer around the brain that prevents germs, infections, and other toxins from getting in. But it also blocks some chemotherapy drugs like methotrexate from reaching the brain.

For induction therapy, high-dose methotrexate is often given together with the immunotherapy drug rituximab (Rituxan). Rituximab can be given on its own, but it usually works better when given with chemotherapy.

In addition to methotrexate and rituximab, one or more other chemotherapy medicines may be part of your treatment.

Other chemotherapy drugs for induction therapy include temozolomide, vincristine, procarbazine, cytarabine, and thiotepa.

Alternatives to methotrexate

High-dose methotrexate (with or without additional medicines) is the preferred induction therapy for primary CNS lymphoma. But it's not the best option for everyone. Your treatment team may recommend a different induction therapy if:

- Your kidneys aren't working well
- High-dose chemotherapy is too intense or too risky for you
- Lymphoma was found in your spine or spinal fluid
- Lymphoma was found in your eye

Whole-brain radiation therapy

If you're unable to have chemotherapy or another anticancer medicine, whole-brain radiation therapy (WBRT) may be an option for induction treatment.

Supportive care

Supportive care is available for everyone with cancer. It isn't meant to treat the cancer, but rather to relieve symptoms and make you more comfortable. Speak to your care team about how you're feeling and if you're having any symptoms or side effects.

For more information on supportive care, see *Chapter 5: Follow-up care and further treatment*.

Second phase of treatment

The purpose of the second (consolidation) phase of treatment is to kill any lymphoma cells that may be left behind after induction and to prevent them from coming back.

Not everyone with primary CNS lymphoma needs consolidation treatment.

If you're having second-phase treatment, you'll have a few tests beforehand, such as imaging and blood tests, to find out how well your first-phase treatment worked.

The results of your first-phase treatment will guide your options for your second-phase treatment.

First-phase result: No signs of lymphoma

If there are no signs of lymphoma after first-phase (induction) therapy, you've had a complete response.

The next best outcome is an unconfirmed complete response, which means that there are minimal signs of lymphoma left in the body.

If you have a complete response or unconfirmed complete response to induction therapy, you may have several options for second-phase (consolidation) therapy. These options are listed in **Guide 3** and described here.

High-dose chemotherapy with stem cell transplant

In people who are healthy and strong enough, high-dose chemotherapy and a stem cell transplant is an option for consolidation.

The preferred chemotherapy combinations are:

- Cytarabine and thiotepa followed by carmustine and thiotepa
- Thiotepa, busulfan, cyclophosphamide, and mesna (a drug that reduces bleeding in the bladder, which can be a side effect of cyclophosphamide)

However, if you have a higher risk of infection or your body can't handle a stem cell transplant for other reasons, high-dose chemotherapy with a stem cell transplant may not be a good option for you.

High-dose chemotherapy

Chemotherapy without a stem cell transplant may be a better fit for someone who isn't suited for a stem cell transplant.

For this consolidation option, the recommended treatment is high-dose cytarabine with or without etoposide. Etoposide is a chemotherapy drug often used in combination with other chemotherapy drugs.

Guide 3
Second-phase (consolidation) treatment for primary CNS lymphoma

Types of treatment	Drugs used in the treatment
No signs of lymphoma after first-phase treatment	
High-dose chemotherapy and stem cell transplant	High-dose Cytarabine and Thiotepa, followed by Carmustine and Thiotepa, then stem cell transplant
	Thiotepa, Busulfan, Cyclophosphamide, and Mesna, then stem cell transplant
High-dose chemotherapy	High-dose Cytarabine and Etoposide
	High-dose Cytarabine
Low-dose whole-brain radiation therapy	Temozolomide (after radiation therapy)
Monthly maintenance therapy	High-dose Methotrexate and Leucovorin, plus Rituximab
	High-dose Methotrexate and Leucovorin
Some lymphoma remaining after first-phase treatment	
High-dose chemotherapy (not Methotrexate)	High-dose Cytarabine and Etoposide
	High-dose Cytarabine
Whole-brain radiation therapy	Temozolomide (after radiation therapy)
Supportive care	Treatment for side effects of lymphoma therapy
	Treatment for symptom relief

Maintenance therapy

You might receive maintenance therapy as your consolidation treatment. Maintenance therapy is given continuously to keep the lymphoma under control or prevent it from coming back. It's typically given once a month for up to 1 year.

Maintenance therapy for primary CNS lymphoma includes high-dose methotrexate and leucovorin with or without rituximab.

Rituximab alone may also be used for maintenance therapy.

Radiation therapy

If more chemotherapy seems too harsh or isn't recommended for other reasons, low-dose WBRT may be an option. Lower doses of radiation cause fewer side effects. So a lower dose is typically used when WBRT is given for consolidation.

First-phase result: Some lymphoma cells remaining

If results show that lymphoma cells remain after methotrexate-based first-phase (induction) therapy, you've had an incomplete response.

The next step is to consider a different treatment to kill leftover cancer cells, prevent neurological damage, and maintain quality of life. These options are listed in **Guide 3** and discussed here.

High-dose chemotherapy

You could have a different chemotherapy medicine than methotrexate for your consolidation treatment. The recommended chemotherapy is high-dose cytarabine either alone or with another chemotherapy drug called etoposide.

Radiation therapy

If you want to avoid more chemotherapy or if chemotherapy is no longer a good option for you, WBRT is recommended. Although radiation therapy has risks, it can relieve symptoms and may control the lymphoma for a while.

Supportive care

If your body isn't able to handle either chemotherapy or WBRT, supportive care is always an option. Supportive care can help with cancer-related pain and discomfort as well as the side effects of treatment.

A remission is when there are no symptoms or signs of cancer after treatment.

Treatment for the spine

If testing finds cancer cells in the spine or spinal fluid and if treatment with high-dose methotrexate is thought to be too harsh for you, your care team may recommend intrathecal treatment as induction therapy.

Intrathecal treatment is chemotherapy injected directly into the spine. Intrathecal chemotherapy options for primary CNS lymphoma include methotrexate, cytarabine, or rituximab.

In addition to intrathecal treatment, you might also have radiation therapy to the spine.

Treatment for the eyes

If tests find lymphoma cells in the eyes, specialized treatment is needed. Recommended treatments include intraocular (eye) chemotherapy, radiation therapy, or standard (whole-body) chemotherapy for primary CNS lymphoma.

Intraocular chemotherapy involves injecting anticancer medicine, such as a high dose of methotrexate, directly into the eyes. For this procedure, you may need to go to an ophthalmologist or another specialist who provides this type of treatment.

If intraocular chemotherapy isn't fully effective or if you can't have this therapy, radiation therapy focused only on the eyes may be an option.

Key points

- Treatment for primary central nervous system (CNS) lymphoma is often a 2-step process that includes an induction phase first and a consolidation phase second. Not everyone needs consolidation therapy.
- The induction phase aims to destroy as many lymphoma cells as possible. The recommended induction treatment (other than a clinical trial) is high-dose chemotherapy plus immunotherapy.
- The consolidation phase kills any cancer cells left behind after the induction phase. Consolidation treatment may also prevent the cancer from returning.
- High-dose chemotherapy and a stem cell transplant may be a consolidation option for people who are healthy and strong enough to have this intense treatment.
- High-dose chemotherapy alone may be a consolidation treatment for those who are unable to have a stem cell transplant.

What is the blood-brain barrier?

Your brain is a very important organ. It needs special protection to keep it safe and healthy. To block germs, infections, and other toxins from getting in, the brain has a unique security system. This protective layer is called the blood-brain barrier. It's like a moat that surrounds and protects a castle.

The blood-brain barrier does its job well—maybe too well. One problem with the barrier is that it won't permit most drugs in the bloodstream to reach the brain. This includes many chemotherapy drugs. However, scientists have learned that some chemotherapy drugs can cross the blood-brain barrier more easily than others.

Questions to ask

- What is your experience as well as your team's experience with treating the type of lymphoma I have?
- Are my chances any better with one treatment than another? Less time-consuming? Less expensive?
- How will you know if the treatment is working?
- What are my options if the treatment stops working?

What's next?

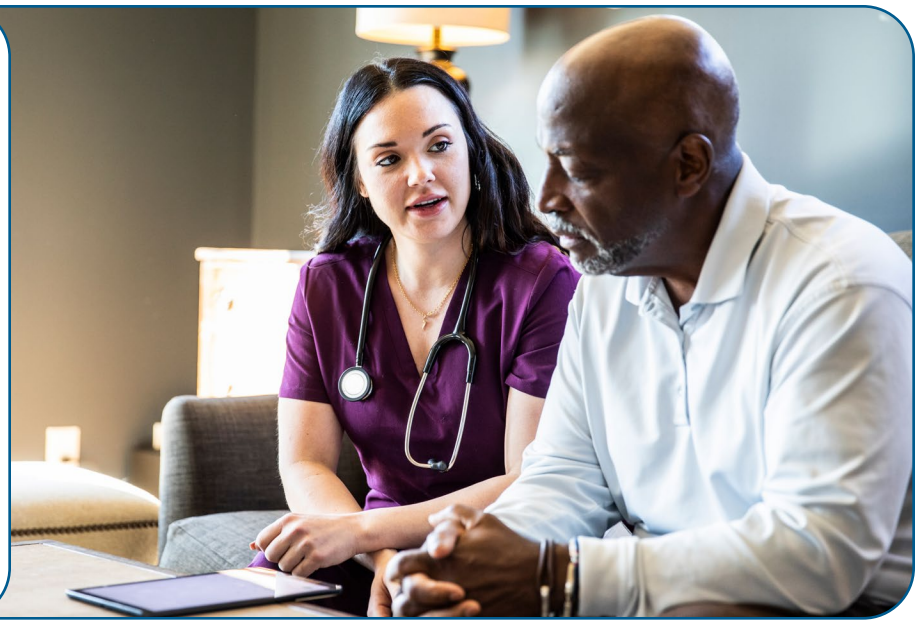
After induction and consolidation therapy, your primary CNS lymphoma may be undetectable for months or perhaps years. Try to relax a little, if you can, and enjoy the break from treatment.

Meanwhile, you'll continue to have regular imaging tests and checkups to see if the lymphoma shows signs of coming back.

When cancer comes back after a period of remission, it's called a relapse. Lymphoma that remains (or gets worse) after treatment is called refractory. Read about relapsing and refractory lymphoma in the next chapter.

Treatment can slow down lymphoma's growth, reduce its symptoms, and prolong life.

With current treatments, some people have achieved long-lasting remission with no signs or symptoms of primary CNS lymphoma.



5

Follow-up care and further treatment

41 Follow-up care

41 If lymphoma remains or returns

43 Further treatments

43 Stopping treatment

43 Supportive care

44 Advance care planning

45 Key points

45 Questions to ask

After you've finished treatment, it's important to go to follow-up visits to check that the cancer hasn't returned. If the lymphoma returns, or didn't go away, you have several options for further treatment.

Follow-up care

After treatment ends, the follow-up phase of care begins. It's important to go to follow-up visits and stay in touch with your treatment team. Follow-up care is for:

- Making sure the lymphoma is in remission
- Watching for signs that the lymphoma may be coming back
- Checking for any unexpected problems related to the lymphoma or treatment

A key test during follow-up of primary central nervous system (CNS) lymphoma is brain imaging with MRI. Brain imaging monitors for the return of the lymphoma. NCCN experts recommend follow-up MRIs of the brain:

- Every 3 months for the first 2 years
- Every 6 months for the following 3 years
- Once a year after 5 years

You may need to have brain MRIs more or less often than this. Your treatment team will explain how often you should expect to have them.

Follow-up after spinal treatment

If cancer cells were found in your spine or cerebrospinal fluid (CSF), your follow-up care may also include MRI scans of your spine or testing your spinal fluid.

Follow-up after ocular treatment

If you received treatment to your eyes for ocular lymphoma, you'll continue to have eye exams with an ophthalmologist or other specialist as part of your follow-up care.

If lymphoma remains or returns

Lymphoma that remains and doesn't improve with treatment is called refractory. Refractory is another word for resistant—the lymphoma has become resistant to treatment.

A relapse is when cancer returns after a cancer-free period.

There is no single best way to treat refractory or relapsed primary CNS lymphoma. The best treatment is the one that's best for you. You'll need to consider your quality of life and how treatment and its side effects may impact it.

For some people, especially those at higher risk of complications, the best option may be no therapeutic treatment at all.

Also keep these 2 options in mind:

- **Clinical trial** – Seeking treatment in a clinical trial is strongly encouraged for relapsed or refractory primary CNS lymphoma. The treatment you receive may or may not work better than standard cancer care. Ask your care team if they can help you find current clinical trials you may be eligible for.
- **Supportive care** – Supportive care is for cancer-related pain or discomfort as well as medication-related side effects. The goal of supportive care is not to treat the lymphoma itself but to help with the physical, emotional, and practical demands of living with cancer.

Other treatment options depend in part on **your previous treatment or treatments.**

If you had whole-brain radiation therapy

If cancer remains or returns after initial whole-brain radiation therapy (WBRT), you should avoid having WBRT again because of the risk of damage to the nervous system.

The only type of radiation therapy that may be given after initial WBRT is in-field radiation (also called focal radiation). This is radiation that focuses only on cancerous areas of the brain, not the whole brain. In-field radiation is given mainly to relieve symptoms, not to treat the cancer.

Your treatment team may recommend chemotherapy instead. Alternative chemotherapies—or anticancer medicines such as rituximab, ibrutinib, or others—may be added or substituted for methotrexate.

High-dose chemotherapy with a stem cell transplant may also be an option in certain cases.

If lymphoma is found in your spine or CSF, you may have chemotherapy injected directly into the spinal fluid.

If you had high-dose chemotherapy

If you had high-dose methotrexate-based chemotherapy that resulted in a long remission (more than 1 year), your care team may recommend that you have it again. It's common to have the same type of chemotherapy you had the first time around.

High-dose methotrexate can be given by itself or with other chemotherapies. Treatment that doesn't include high-dose methotrexate is also an option.

If high-dose methotrexate-based chemotherapy didn't work or didn't result in a lasting cancer-free period, there's more than one other option. Your team may recommend chemotherapies or other anticancer treatment that doesn't include methotrexate.

Another option is radiation therapy—either WBRT or in-field radiation—with or without other chemotherapy or anticancer treatment.

High-dose chemotherapy with a stem cell transplant may also be an option for people who can tolerate it.

If you had high-dose chemotherapy with stem cell transplant

If high-dose chemotherapy with a stem cell transplant led to a complete remission that lasted 1 year or more, your treatment team may suggest you have it again.

If that's too much or not possible for you, then another option is chemotherapy or other anticancer therapy that doesn't include methotrexate or a stem cell transplant.

If you didn't have a lasting response to high-dose chemotherapy with a stem cell transplant, radiation therapy may be an option. WBRT or in-field (focal) radiation may be used.

Further treatments

You may have several types of treatment for relapsed or refractory primary CNS lymphoma. After any treatment, it's important to go to follow-up visits.

Stopping treatment

You may reach a point where you want to stop lymphoma treatment. For some people, how they spend their time is more important than how much time they have left.

Supportive care

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment.

Supportive care is for everyone with cancer and their families, not just for those at the end of life. It's also known as palliative care.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

Read more about the types of support you may receive in *NCCN Guidelines for Patients: Palliative Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Advance care planning

Advance care planning is for anyone with lymphoma, not just for people who are very sick. Even when lymphoma is curable, talking about future scenarios should start when treatment starts.

Advance care planning means deciding what care you would want if you become unable to make medical decisions for yourself. It's about making sure that your wishes are understood and respected.

You can decide if there's a point where you might want to stop lymphoma treatment. You can also decide what treatments you would want for symptom relief.

You can speak to your care team to set up an advance care plan early on, so you'll feel less stressed and better able to cope with your condition.

Your comfort and quality of life shouldn't come second to excessive tests and procedures that won't affect your outcome.

"Report any unusual feelings of sadness, loss of interest in activities, anxiety, and sleep problems to your doctor. Many people experience these feelings, and they should not go untreated."



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

NCCN.org/patients/comments

Key points

- Follow-up visits are for making sure the lymphoma is in remission. Follow-up also looks for signs of its return and checks for any unexpected problems.
- Cancer that doesn't improve with treatment is called refractory. Cancer that returns after a cancer-free period is known as a relapse.
- Trying to enroll in a clinical trial is strongly encouraged for everyone with relapsed or refractory primary central nervous system (CNS) lymphoma.
- If your initial treatment was whole-brain radiation therapy, the usual therapy for relapsed or refractory CNS lymphoma is methotrexate-based chemotherapy. High-dose chemotherapy with a stem cell transplant is another possible treatment.
- If your initial treatment was high-dose methotrexate chemotherapy and you had a remission that lasted more than 1 year, the therapy for relapsed or refractory disease may be more methotrexate chemotherapy. This may be given by itself or with other medicines.
- Supportive care is for relieving the symptoms of cancer and the side effects of cancer treatment.
- Supportive care is appropriate for any person with cancer, regardless of age, cancer stage, or the need for other therapies.

Questions to ask

- Who can help me find a clinical trial that suits me?
- What further treatment can I have if my first treatment for relapsed or refractory CNS lymphoma doesn't work?
- Will my insurance pay for the treatment or treatments you're recommending?
- What will happen if I stop treatment at this stage?

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Other resources

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Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- The details of lymphoma treatment and its side effects
- Finding a specialist who's experienced in brain tumors
- Being a part of the care team
- How to get a second opinion
- Getting financial help
- Finding an appropriate clinical trial
- Coping with other health problems

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

AnCan Foundation
ancan.org

Blood & Marrow Transplant Information Network (BMT InfoNet)
bmtinfonet.org

Blood Cancer United
bloodcancerunited.org

Cancer*Care*
cancercare.org

Imerman Angels
imermanangels.org

Lymphoma Research Foundation
lymphoma.org

National Bone Marrow Transplant Link (nbmtLINK)
nbmtlink.org

NMDP
nmdp.org

Stupid Cancer
stupidcancer.org

Triage Cancer
triagecancer.org

Questions to ask

- Who should I contact with questions or concerns during weekends or non-office hours?
- What supportive care services are available to me during and after treatment?
- How can I connect with others and build a support system?
- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?



Let us know what you think!

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



Words to know

biopsy
A procedure that removes samples of tissue or fluid to be tested for disease.

blood-brain barrier
A cell network that blocks harmful substances but allows nutrients from the blood to enter the central nervous system.

bone marrow biopsy
A procedure that removes samples of bone and marrow to be tested for disease.

central nervous system (CNS)
The brain and spinal cord.

cerebrospinal fluid (CSF)
A liquid that flows in and around the hollow spaces of the brain and spinal cord. Also called spinal fluid.

chemotherapy
Drug treatment that damages and destroys rapidly dividing cells throughout the body.

clinical trial
A type of research that assesses investigational tests or treatments in people.

consolidation therapy
The second phase of treatment, which is given to kill any cancer cells left in the body after initial (induction) therapy.

follow-up care
Health care that involves regular checkups, which begin after treatment has ended.

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

immunotherapy
Drug treatment that helps the body's immune system find and destroy cancer cells.

induction therapy
The first phase of treatment, which aims to destroy as many cancer cells as possible.

in-field radiation therapy
Radiation therapy given only to the lymphoma, not the whole brain. Also called focal radiation.

lymphoma
Cancer that begins in white blood cells (lymphocytes) that are part of the immune system. The cells grow out of control.

radiation therapy
Treatment that uses high-energy rays (radiation) to kill cancer cells.

refractory cancer
Cancer that does not improve with treatment.

relapse
The return of cancer after a period of improvement.

remission
The absence of cancer signs and symptoms after treatment.

slit-lamp eye exam
An exam that uses a microscope and a strong beam of light to inspect the inside of the eye.

spinal tap
A procedure that removes a small amount of cerebrospinal fluid for testing. Also called a lumbar puncture.

stem cell transplant
Cancer treatment that uses high-dose chemotherapy to destroy cells in the bone marrow, which are replaced with healthy blood stem cells. Also called a stem cell rescue.

stereotactic biopsy
A procedure that removes a tissue sample using a thin, hollow needle guided by a computerized navigation system.

supportive care
Health care for the symptoms of cancer or for the side effects of cancer treatment. Also called palliative care.

targeted therapy
Drug treatment that identifies and attacks a specific feature of cancer cells with less harm to normal cells.

tumor
A mass of abnormal cells. A tumor is the same as cancer.

whole-brain radiation therapy (WBRT)
Cancer treatment that sends small amounts of radiation to the whole brain, including tumors and healthy tissue.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers, Version 2.2026. It was adapted, reviewed, and published with help from the following people:

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City of Hope National Medical Center
Duarte, California

Dana-Farber Cancer Institute
Boston, Massachusetts

Duke Cancer Institute
Durham, North Carolina

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Philadelphia, Pennsylvania

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska

Fred Hutchinson Cancer Center
Seattle, Washington

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Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota

Memorial Sloan Kettering Cancer Center
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The University of Texas MD Anderson Cancer Center
Houston, Texas

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UC San Diego Moores Cancer Center
La Jolla, California

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California

UCSF Helen Diller Family Comprehensive Cancer Center
San Francisco, California

University of Colorado Cancer Center
Aurora, Colorado

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

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Primary Central Nervous System Lymphoma

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