

# CNS lymphoma

Lymphoma can sometimes affect the central nervous system (the brain, spinal cord and eyes). This information explains more about this and how it may be treated.

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# Quick overview

**This section is an overview of the information on this page. You can read only this section or read more detail in the sections below.**

## What is it?

Lymphoma that affects the brain, spinal cord or eyes can be found only in these areas (primary CNS lymphoma) or can spread there from other parts of the body (secondary CNS lymphoma).

## What are the symptoms and how is it diagnosed?

Symptoms, such as muscle weakness, can affect particular areas of the body. You might have headaches, seizures (fits) or problems with your vision or balance. Some people have mild, vague symptoms; for example, feeling confused or finding it difficult to concentrate. You need urgent treatment if you have spinal cord compression (lymphoma is pressing on your spinal cord) or intracranial hypertension (high pressure around your brain).

You need scans and a biopsy (a sample of the abnormal area is taken) to confirm you have CNS lymphoma. You are likely to have other tests too to find out how the lymphoma is affecting you.

## How is it treated?

Many people have steroids initially to reduce swelling and symptoms. Chemotherapy drugs that can reach the CNS are usually given either intravenously (into a vein) or intrathecally (into the CNS by lumbar puncture). The antibody treatment rituximab may also be given. If chemotherapy is successful, some people then have radiotherapy to their whole brain or an autologous stem cell transplant, which is a treatment that allows you to have stronger chemotherapy. These treatments are given to reduce their risk of relapse (lymphoma coming back).

# What is central nervous system lymphoma?

**Lymphoma** that is found in the CNS is called 'CNS lymphoma'. CNS lymphomas are uncommon forms of **non-Hodgkin lymphoma**.

CNS lymphoma most commonly affects the brain. Around 1 in 50 brain tumours are a type of CNS lymphoma.

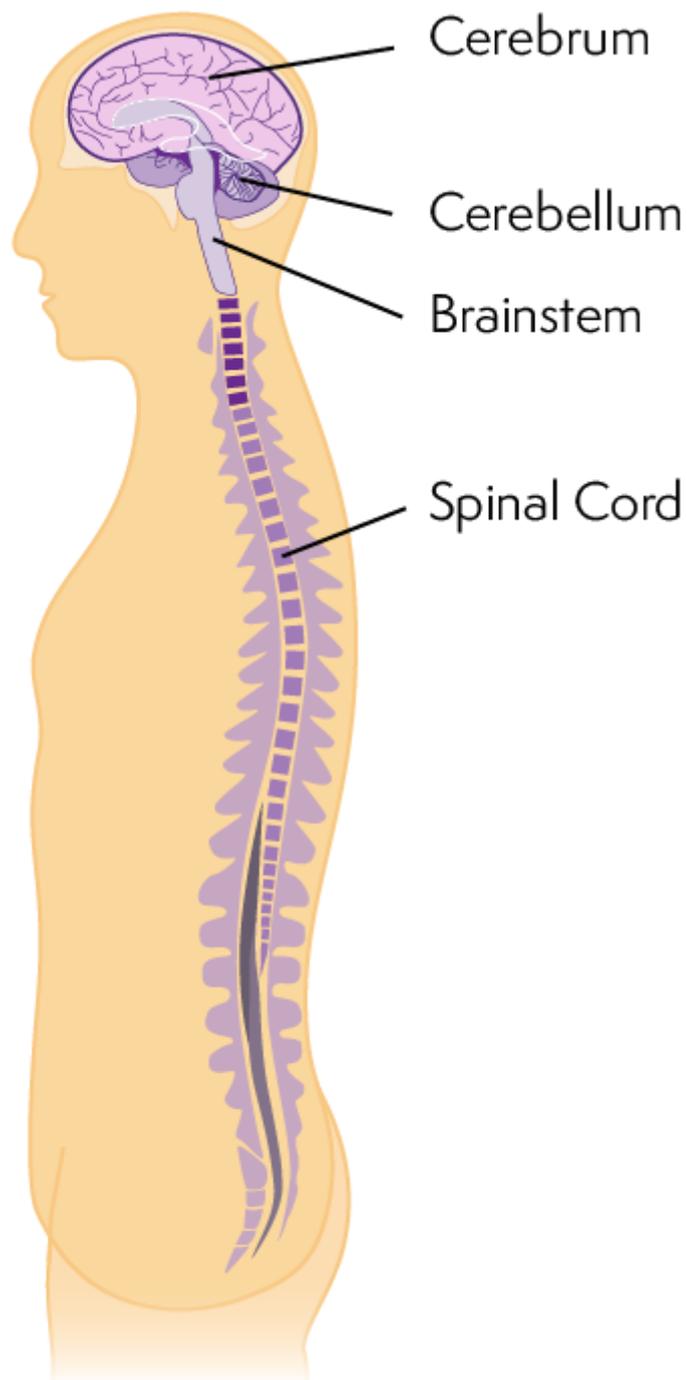
## What is the central nervous system?

The CNS is the part of the body that controls all body functions. It includes the brain, spinal cord and eyes.

The **brain** is made up of:

- the **cerebrum**, which controls our speech and understanding, our sensation and voluntary movement (movements we decide to make)
- the **cerebellum**, which helps with movements and controls our balance
- the **brainstem**, which controls essential body functions, such as our breathing, heart rate and blood pressure.

The **spinal cord** runs from the brain down the back within the bones of the spine. A series of nerves join directly onto the spinal cord. The nerves carry information about sensation from around the body and transmit messages to control the muscles of the body.



**Figure: Diagram of central nervous system**

Your CNS is protected from the rest of your body in several ways.

- The **meninges** are protective layers of tissue that cover the brain and spinal cord – this is what becomes inflamed in ‘meningitis’.

- A special fluid called '**cerebrospinal fluid**' (**CSF**) surrounds the brain and spinal cord to cushion them. It is found in the space between the meninges and the brain and spinal cord.
- The **blood-brain barrier** surrounds the brain. It is a barrier of cells and blood vessels that only lets certain substances reach the brain to protect it from harmful chemicals and infections. It also prevents or interferes with many chemotherapy drugs passing from the blood to the brain.

This protection is very important but it prevents many drugs from reaching lymphoma in the CNS.

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## Types of CNS lymphoma

Lymphoma in the CNS is usually high-grade (fast-growing) and is most often a form of **diffuse large B-cell lymphoma**. Low-grade (slow-growing) lymphoma can also develop in or around the brain, but only around 1 in 20 cases of CNS lymphoma are a low-grade lymphoma.

There are different types of CNS lymphoma that affect different parts of the CNS.

- **Primary CNS lymphoma (PCNSL)** usually develops as one or more lumps in the brain.
- Primary CNS lymphoma can affect the eyes ('**intraocular lymphoma**'). In most cases, the lymphoma is in other parts of the CNS as well as the eyes. If lymphoma is found only in the eyes, it is called '**primary intraocular lymphoma**'.
- **Secondary CNS lymphoma** is lymphoma that started elsewhere but has spread to the CNS or has relapsed (come back) in the CNS.
- **Diffuse meningeal lymphoma** is lymphoma that is spread out (diffuse) only within the **meninges** rather than forming a lump. It is usually a form of secondary CNS lymphoma.

It is very uncommon for CNS lymphoma to develop in the spinal cord. However, other types of lymphoma can affect the spinal cord by pressing on it, causing **spinal cord compression**. Spinal cord compression can happen with most types of lymphoma, but it is rare.

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# Who gets CNS lymphoma and what causes it?

Primary CNS lymphoma is an uncommon form of lymphoma. The average age at diagnosis is around 60. It is slightly more common in people who have a weakened immune system, which might be caused by:

- **HIV (human immunodeficiency virus)** infection – this is much less common now that good antiviral treatments are available
- drugs that are used to suppress the immune system following an **organ transplant**, or other types of immunosuppressive treatment, for example, for rheumatological conditions.

Low-grade lymphomas in the CNS, such as MALT lymphoma, are rare and usually occur in younger people.

Secondary CNS lymphoma is lymphoma that has spread to the CNS from elsewhere in the body. People with the fastest-growing types of high-grade non-Hodgkin lymphoma (NHL), for example, **Burkitt lymphoma**, are at the highest risk of developing secondary CNS lymphoma. Some people diagnosed with high-grade NHL are offered treatment that aims to prevent the spread of lymphoma to the CNS. This treatment is called '**CNS prophylaxis**'.

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## Symptoms

The **symptoms** of CNS lymphoma depend on where the lymphoma is and how much lymphoma there is in your body.

### Symptoms of primary and secondary CNS lymphoma

Symptoms can include:

- muscle weakness in a particular area, for example, in one limb

- loss of sensation in a particular area
- changes in vision or a partial loss of vision
- seizures (fits)
- headache
- nausea and vomiting
- problems with balance.

My left arm stopped working. Within a couple of hours it felt fine, but during dinner I suddenly lost the use of my left arm again and dropped my fork. On the way to hospital, I had a kind of seizure. I remained conscious throughout, but my limbs were jerking and I was thrashing around in the front seat of the car. I couldn't speak and was struggling to swallow. I was aware of what was happening, but couldn't do anything about it.

– Roger, diagnosed with primary CNS lymphoma  
at 48

Some less obvious symptoms can develop. These can come on gradually and may be difficult to pick up at first. In older people, some of these symptoms could be confused with ageing or other problems. These symptoms include:

- vague confusion
- increased irritability and other changes in personality
- poor attention (decreased ability to concentrate)

- expressive dysphasia, which is difficulty finding the right word even though this might be something quite simple.

Lymphoma in certain areas of the brain could block the flow of **CSF**. The build-up of CSF can cause intracranial hypertension – an increase in pressure around the brain. Symptoms of intracranial hypertension include:

- a change in consciousness (becoming drowsy and unresponsive)
- headaches
- vomiting.

Lymphoma causing intracranial hypertension needs urgent treatment.

## Symptoms of intraocular lymphoma

The lymphoma can affect one or both eyes in some people. Not everyone with CNS lymphoma involving the eye notices a change in their vision but common symptoms include:

- blurred vision
- floaters (small dots or spots that seem to float quickly across your vision).

In most cases, lymphoma is found in the eye and in other parts of the CNS. People can therefore have a mixture of symptoms. Rarely, only the eye is affected (primary intraocular lymphoma).

## Symptoms of diffuse meningeal lymphoma

Diffuse meningeal lymphoma causes similar symptoms to other CNS lymphomas. The symptoms may be milder and less obvious than those that occur when there is a lump of lymphoma.

## Symptoms of spinal cord compression

Spinal cord compression due to lymphoma pressing on the spinal cord can cause a range of symptoms depending on where the spine is being compressed. These can include:

- weakness and, in some cases, paralysis, most often affecting the legs but sometimes also the arms or chest/abdomen (tummy)
- loss of sensation or a change in sensation, most often affecting the legs but sometimes also the arms or chest/abdomen
- a change in bowel function (for example, constipation) or bladder function (for example, not being able to pass urine)
- a loss of sensation around the anus (bottom)
- back pain.

If you have symptoms of spinal cord compression, let a member of your medical team know immediately. It is important that it is diagnosed urgently. Prompt treatment gives you a better chance of your nerves recovering well.

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## Diagnosis and staging

Several different tests can be used to diagnose and find out more about CNS lymphoma. It is important that you are diagnosed correctly as other tumour types are treated differently.

Different types of **scan** can be used to find CNS lymphoma in the body:

- magnetic resonance imaging (MRI) scans, which usually give the best images of the brain and other parts of the CNS and can also detect spinal cord compression
- computed tomography (CT) scans, which are usually used to detect lymphoma elsewhere in the body, but may be used to look at the bones of the spine
- positron emission tomography (PET) scans, which are often used in combination with a CT scan to detect active lymphoma elsewhere in the body.

To diagnose lymphoma, you need a **biopsy**.

- If the lymphoma is in another part of your body as well as in your CNS, the biopsy is likely to be taken from outside the CNS.

- If the lymphoma is only in your brain, a neurosurgeon (specialist in diagnosing and treating problems with the CNS) takes a brain biopsy.
- If the lymphoma is only in your eye, an ophthalmologist (specialist in diseases and injuries of the eye) may take a little of the vitreous (the gel-like substance inside your eye) to check for lymphoma cells.
- If there is lymphoma in your spine, a specialist radiologist may take a biopsy from your spine.

Before the test, your medical team should discuss the procedure with you.

Lumps within the brain are biopsied using CT scanning to help guide the biopsy needle to the right area. This is called 'stereotactic biopsy'. You are likely to have a general anaesthetic for your biopsy as it is very important you do not move.

You also have **blood tests** as part of your diagnosis and throughout your **treatment** and **follow-up**. These may include a test for HIV. People with HIV are more likely to develop some types of lymphoma, including CNS lymphoma. Most people with CNS lymphoma do not have HIV. However, it is important to find out if you do have HIV. If you do, you need treatment for both the lymphoma and the HIV because the outcome is better with combined treatment.

Other tests that may be done include:

- a specialist eye examination to check for lymphoma in your eyes; eye tests are usually done in an ophthalmology department at the hospital
- a **lumbar puncture** to take a sample of your **CSF** to look for lymphoma cells
- a testicular **ultrasound scan** for men
- a **bone marrow biopsy** to look for lymphoma cells in your bone marrow (the spongy tissue in the centre of your bones where blood cells are made).

Not everyone needs all the tests described here and you may need other **tests**. Your medical team decide what tests you need based on your individual circumstances.

Although **waiting for the results** of your tests can be difficult, your doctor is collecting important information during this time. It is important that your doctor knows exactly how your lymphoma is affecting you so they can give you the most appropriate treatment.

## What does 'stage' mean?

'**Staging**' is the process of working out how widespread your lymphoma is and how it is affecting you.

There is no established staging system for primary CNS lymphoma as it tends to stay in the CNS. However, your tests are still important in finding out how the lymphoma is affecting you and in identifying risk factors that could affect your prognosis (outlook). These factors can be important in deciding on the best treatment for you.

Secondary CNS lymphoma is a high-grade lymphoma that starts elsewhere and spreads to the CNS. It is staged like other high-grade lymphomas from 1 to 4, where 1 is localised (in one place) and 4 is the most widespread lymphoma.

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## Outlook

Survival statistics can be confusing as they don't tell you what your individual outlook is – they only tell you how a group of people with the same diagnosis did over a period of time in the past.

Treatment strategies for CNS lymphoma have improved greatly over recent years. However, CNS lymphomas can still be difficult to treat. Some treatments have a risk of causing long-term neurological problems (problems with your brain and nerves). These problems become more likely the older you are when you are diagnosed with CNS lymphoma. Your medical team balance the chance of remission with the risk of long-term problems when recommending a treatment.

Your doctor is best placed to advise you on your outlook based on your individual circumstances. Your doctor can use the results of your tests and consider other factors, like your age, symptoms, and other conditions you

might have to predict how likely you are to respond to a particular treatment. These factors are called 'risk factors'.

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## Treatment

Your medical team recommend treatments based on several factors, including:

- what type of CNS lymphoma you have
- where the lymphoma is growing
- how it is affecting you
- how urgently you need treatment
- your age and your general health.

Different types of CNS lymphoma are treated differently.

## Treatment for primary CNS lymphoma

The first treatment for primary CNS lymphoma is often **steroids**. These can help to reduce oedema (swelling) in the tissues around the lymphoma, reducing symptoms. They can also shrink the lymphoma, at least for a short time, while other treatments are arranged.

Most people with primary CNS lymphoma are then treated with **chemotherapy** that crosses the blood-brain barrier. The antibody treatment rituximab might be added to chemotherapy.

If the lymphoma responds to chemotherapy, your medical team is likely to suggest **whole-brain radiotherapy** or an **autologous stem cell transplant**. These are consolidation treatments, which means they are used to reduce the risk of relapse after successful treatment.

Low-grade CNS lymphomas are rare. They usually respond very well to treatment, typically **radiotherapy**. Sometimes surgery to remove the lump is all that is needed for low-grade CNS lymphomas.

### **Steroids**

**Steroids** are usually started after any biopsies have been taken because the lymphoma can be harder to diagnose once you have had steroids. Your specialist might suggest starting steroids straightaway if you are very likely to have CNS lymphoma, particularly if it is causing lots of problems.

Steroids can be given orally (by mouth) or intravenously. The most common steroid used for CNS lymphoma is dexamethasone.

Side effects of steroids that can be a particular problem for people with CNS lymphoma include:

- difficulty sleeping because the steroids often have to be given throughout the day rather than just in the morning
- increased blood sugar levels because a high dose of steroids is often needed, especially at first
- changes in mood and behaviour – these may be confused with the symptoms of CNS lymphoma.

## **Chemotherapy**

**Chemotherapy** is the main way of treating primary CNS lymphoma that is caused by high-grade lymphoma. The regimens (combinations of drugs) used include drugs that are more likely to cross the **blood–brain barrier**, such as high-dose methotrexate.

High-dose methotrexate is given by intravenous infusion (drip) over a few hours. It is often given as an inpatient treatment because you need to have lots of fluids before and afterwards. It is sometimes possible for the treatment to be given through a special pump, which allows people to spend some of their time at home ('ambulatory chemotherapy'). You have regular blood tests and urine tests to check how the treatment is affecting your body.

You are given other treatments to help support your body during your chemotherapy, for example sodium bicarbonate and folic acid, which can reduce the side effects of methotrexate. The time you have to stay in hospital varies depending on how fit you are and how your body reacts to the treatment.

Methotrexate is often given with other chemotherapy drugs, such as high-dose cytarabine, and with **antibody treatments**, such as **rituximab**. For example, the MATRix regimen might be used:

- methotrexate
- cytarabine
- rituximab
- thiotepa.

A number of different regimens can be used – your medical team can tell you exactly which drugs they recommend and what your treatment involves.

New drugs continue to be tested in various regimens and **clinical trials** are ongoing.

## **Radiotherapy**

**Radiotherapy** for primary CNS lymphoma is usually targeted against all of the brain. This is known as ‘whole-brain radiotherapy’. Whole-brain radiotherapy is usually used as a consolidation treatment after chemotherapy.

Consolidation treatments aim to reduce the risk of relapse (lymphoma coming back). Radiotherapy is sometimes used on its own for people who are not fit enough to have chemotherapy. It might also be used on its own for primary CNS lymphoma that is due to a low-grade lymphoma.

Your medical team can give you more information about your treatment plan if they recommend whole-brain radiotherapy. Most people who have whole-brain radiotherapy have the treatment 5 days a week for 2–4 weeks.

The side effects of whole-brain radiotherapy can include:

- worsening of your symptoms in the early stages of treatment
- fatigue – this might take some months to improve after treatment
- poor attention
- poor memory
- problems with language
- slowness of thinking, movement and/or speech

- difficulties solving problems, planning and making decisions.

These side effects might be referred to as '**cancer-related cognitive impairment**'.

Some of these problems can develop as late effects months or even years after the treatment. These problems are more likely the older you are when you are treated.

### **Stem cell transplants**

Your medical team might suggest an **autologous stem cell transplant** instead of radiotherapy if chemotherapy has controlled your lymphoma. A stem cell transplant is an intensive form of treatment that is only suitable for those fit enough to have it.

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## **Treatment for primary intraocular lymphoma**

Primary intraocular lymphoma is usually treated in the same way as other cases of primary CNS lymphoma. There is a high risk of **relapse** in the CNS if only the eye is treated.

**Chemotherapy** directly into the eye ('intravitreal' chemotherapy) is sometimes given to people who are not fit enough for high doses of intravenous chemotherapy or for lymphoma that has relapsed in the eye.

Most people have chemotherapy that includes high-dose methotrexate (with or without other drugs) followed by a **stem cell transplant** and/or **radiotherapy**. Radiotherapy is usually given to both eyes and may also be directed at the brain even if there is only evidence of lymphoma in one eye.

Side effects of radiotherapy to the eyes can include:

- temporary loss of your eyelashes
  - dry eyes
  - cataracts (you might need to have cataract surgery in the future)
  - glaucoma.
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## Treatment for secondary CNS lymphoma

Secondary CNS lymphoma might be found as lumps within the brain or, occasionally, only in the **meninges** (diffuse meningeal lymphoma). Lymphoma can relapse only in the CNS or might be found elsewhere in the body at the same time or shortly after. Symptoms usually develop quickly.

Because secondary CNS lymphoma has spread from elsewhere in the body, treatment is usually given that can reach the CNS and the rest of the body. If you are fit enough, this might be high-dose **chemotherapy** including drugs that can reach the CNS. This is sometimes called 'salvage' chemotherapy.

Salvage chemotherapy often includes **intrathecal chemotherapy**, where chemotherapy is injected directly into the CNS during a **lumbar puncture**. Only a limited number of drugs, including methotrexate, cytarabine and hydrocortisone (a steroid), can be safely given this way.

If you are having your chemotherapy intrathecally, you may have it given through an Ommaya reservoir, which is a plastic device placed under your scalp. It avoids the need for repeated lumbar punctures.

If chemotherapy controls the lymphoma, you might be able to have a **stem cell transplant** to give you a better chance of remission (no evidence of lymphoma).

If you are not fit enough for chemotherapy or the lymphoma does not respond to it, your doctor might suggest **palliative** radiotherapy to ease your symptoms.

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## Treatment for diffuse meningeal lymphoma

There is no standard treatment for diffuse meningeal lymphoma. You are likely to have repeated doses of **chemotherapy** that includes high-dose methotrexate. Your chemotherapy may be given intravenously or intrathecally. **Intrathecal chemotherapy** is given directly into the CSF during a lumbar puncture or into an **Ommaya reservoir**.

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# Treatment for spinal cord compression

Your first treatment is likely to be a **steroid** such as dexamethasone. Steroids can help to reduce swelling and ease the pressure on your nerves. They may also shrink the lymphoma for a short time, allowing time for other treatments to be arranged.

Lymphoma within the spine is usually treated in the same way as **primary CNS lymphoma** in other locations, with **chemotherapy** regimens that include high-dose methotrexate. Some people also have **radiotherapy** to the spine.

Lymphoma that is outside the CNS but causing compression by pressing on the spine is treated with the standard treatment for that **type of lymphoma**, such as R-CHOP. Intrathecal chemotherapy or other drugs such as high-dose methotrexate may be added. You may have chemotherapy followed by radiotherapy to the area of spine that was affected.

Surgery may sometimes be used to remove a slowly-growing lymphoma if it is compressing the spinal cord.

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## After treatment

Sometimes, the symptoms of CNS lymphoma resolve quickly with treatment. Initial treatment with steroids can be very effective in relieving symptoms. However, nerve tissues grow very slowly and it can sometimes take a long time for symptoms to improve. Some people see gradual improvement of their symptoms. Some people find their symptoms never resolve completely, especially if they were present for a long time before treatment.

Your medical team can support your recovery by referring you to appropriate specialists.

If you have had muscle weakness and your strength does not recover quickly, physiotherapists and occupational therapists can offer help and advice to improve your quality of life. Their help might also stop your symptoms worsening or other problems developing in the longer term.

Psychologists can offer support if you are having cognitive (thinking) problems, for example with your memory or attention. Psychologists and

counsellors can also support you if you need help with the emotional aspects of your lymphoma.

Once you have finished your treatment, you have regular **follow-up appointments**. These appointments are important in supporting your recovery. Your specialist can check:

- your symptoms are improving in the weeks and months after treatment
- whether any side effects from your treatment have settled
- your quality of life and whether anything can be done to improve it
- whether you develop any problems with **late effects** of your treatment.

It is important that any signs of **relapse** are detected as early as possible so you can have treatment quickly. Your specialist can arrange any **tests or scans** needed to check on your health and to look for signs of the lymphoma relapsing. Contact your medical team if you develop any new or worsening symptoms or have any concerns between follow-up appointments. They can reassure you or arrange to see you earlier if necessary.

Your medical team want to help you live the best life possible after your treatment. Talk to them about any problems you are having and ask about any support on offer.

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## Relapsed or refractory CNS lymphoma

Other treatments might be available if CNS lymphoma relapses or is refractory (doesn't respond) to treatment. The treatment you can have depends on how fit you are at the time, what treatment you had before and how the lymphoma is affecting you. Your specialist can talk through the options with you. Possible treatments include:

- more intense (stronger) chemotherapy, possibly followed by a stem cell transplant
- **targeted drugs** being tested in a clinical trial
- radiotherapy, if you have not already had it

- palliative treatments given with the aim of easing your symptoms.

You can also search our clinical trials information service, [Lymphoma TrialsLink](#) to find clinical trials currently open in the UK for people with CNS lymphoma.

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## Living with and after CNS lymphoma

Illnesses that affect the brain and nerves can be difficult to live with. It is very important that you find the right help if you have CNS lymphoma, or if you are caring for someone with this type of lymphoma.

We offer a range of support services to help you live your life with and after CNS lymphoma:

- a Freephone helpline offering information and support about any aspect of lymphoma. Call us on 0808 808 5555. You can also email at [information@lymphoma-action.org.uk](mailto:information@lymphoma-action.org.uk) or LiveChat via our website.
- local [support groups, forums](#) and a [Buddy scheme](#), so you can get in touch with other people affected by similar conditions
- a Live your Life programme of free support, events and activities for people with a lymphoma diagnosis and their family, carers or friends.

We also have information for people [caring for someone with lymphoma](#).

Our [list of organisations](#) that offer support and information for people with lymphoma might also be useful. The following organisations offer support and information that is particularly relevant for people with CNS lymphoma:

- [The Brain Tumour Charity](#)
- [Brainstrust](#)
- [Brain and Spine Foundation](#)
- [Headway](#)
- [Carers UK](#).

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## References

These are some of the sources we used to prepare this information. The full list of sources is available on request. Please contact us by email at [publications@lymphoma-action.org.uk](mailto:publications@lymphoma-action.org.uk) or phone on **01296 619409** if you would like a copy.

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- Ferreri AJM, et al. Whole-brain radiotherapy or autologous stem-cell transplantation as consolidation strategies after high-dose methotrexate-based chemoimmunotherapy in patients with primary CNS lymphoma: results of the second randomisation of the International Extranodal Lymphoma Study Group-32 phase 2 trial. *Lancet Haematol*. 2017; 4: e510–e523. Available at: [bit.ly/2qay0QF](https://bit.ly/2qay0QF) (Accessed November 2017).

## Further reading

- [Chemotherapy](#)
- [Glossary](#)

- Self (autologous) stem cell transplants

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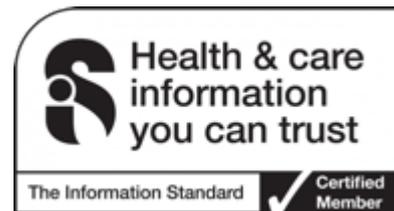
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