CNS prophylaxis

Treatment given to prevent lymphoma spreading to your central nervous system (CNS) is called ‘CNS prophylaxis’. Most people with lymphoma do not need this type of treatment. Your doctor might recommend this preventative treatment if you have certain types of lymphoma or risk factors that could put you at higher risk of your lymphoma spreading to your CNS (brain, spinal cord and eyes).

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‘Prophylaxis’ is a treatment that is designed to prevent something. Central nervous system (CNS) prophylaxis is treatment that aims to stop lymphoma spreading to the brain and spinal cord.

Some types of lymphoma can spread to the CNS from somewhere else. Many chemotherapy regimens (combinations of drugs; for example CHOP) do not reach the CNS. The lymphoma might be treated successfully elsewhere, but
tiny numbers of cells could be present in your CNS and could continue to grow. This can cause the lymphoma to **relapse** (come back) in your CNS.

Lymphoma that is in the CNS but started somewhere else is known as ‘secondary CNS lymphoma’. It can be difficult to treat secondary CNS lymphoma and it can cause long-term neurological (brain and nerve) problems, so doctors sometimes suggest giving treatment to prevent it developing.

Most people with lymphoma have a low risk of secondary CNS lymphoma and do not need CNS prophylaxis. Your medical team will only suggest CNS prophylaxis if you have risk factors that make your lymphoma more likely to spread to the CNS.

You do not have CNS prophylaxis if there is evidence that your lymphoma is already in your CNS. You need more frequent treatment with drugs that reach the CNS if you have **CNS lymphoma**.

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**What is the central nervous system?**

The central nervous system (CNS) is the part of your body that controls all your body’s functions. It includes the brain, the spinal cord and the eyes.
Figure: The brain and spinal cord
Your CNS is protected from the rest of your body.

- A special fluid called ‘cerebrospinal fluid’ (CSF) surrounds the brain and spinal cord to cushion them.
- The blood-brain barrier surrounds your 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 is important that your CNS is protected from harm. However, this protection can make it difficult to treat lymphoma in this area.

Who might need CNS prophylaxis?

CNS prophylaxis is part of the standard treatment for very fast-growing types of lymphoma, which are the most likely types of lymphoma to spread to the CNS. For example:

- **Burkitt lymphoma**
- **lymphoblastic lymphoma**.

**Diffuse large B-cell lymphoma** (DLBCL) can spread to the CNS. However, not everyone with DLBCL has the same risk. Most people with DLBCL do not need CNS prophylaxis. This treatment is offered only to people who have a higher risk of their lymphoma spreading to the CNS.

You are likely to have CNS prophylaxis if DLBCL is in certain areas of your body, for example, in a:

- testicle
- breast
- adrenal gland (glands that produce hormones to help your body function correctly)
- kidney.

You might also be at higher risk of lymphoma spreading to your CNS if the lymphoma is growing close to it, for example at the base of your skull or around your spine.

You might also have CNS prophylaxis if you have several of the following factors that can increase your risk of lymphoma affecting your CNS. The more of these risk factors you have, the greater the risk of lymphoma spreading to your CNS. Your doctor is likely to recommend CNS prophylaxis
if you have four or five of these risk factors, and will consider whether you need CNS prophylaxis if you have two or three risk factors:

- you have high levels of a chemical called 'lactate dehydrogenase (LDH)' in your blood
- you are over 60 years old
- you are particularly unwell when first diagnosed with lymphoma
- your lymphoma is in two or more extranodal sites (two or more places outside of the lymph nodes)
- you have stage 3 or 4 DLBCL.

Many doctors use the same markers of higher risk when treating people with other types of high-grade non-Hodgkin lymphoma, including primary mediastinal large B-cell lymphoma, some types of T-cell lymphoma and transformation of low-grade lymphoma into a faster-growing type of lymphoma.

People with mantle cell lymphoma do not usually need CNS prophylaxis. Your doctor might suggest CNS prophylaxis if they think you could be at higher risk of secondary CNS lymphoma.

It is very uncommon for secondary CNS lymphoma to develop in people with low-grade non-Hodgkin lymphoma or Hodgkin lymphoma. People with these types of lymphoma very rarely need CNS prophylaxis.

Speak to your medical team if you are concerned about your risk of developing secondary CNS lymphoma and whether CNS prophylaxis is suitable for you. Your medical team are best placed to advise you on whether you need CNS prophylaxis. They can also explain the risks and benefits of this type of treatment.

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**How is CNS prophylaxis given?**

The brain is protected from harmful chemicals and infections by the blood–brain barrier: a barrier of cells and blood vessels that only lets certain substances through.
Depending on whether a drug can cross the blood–brain barrier, CNS prophylaxis can be given in two ways:

- **intrathecal chemotherapy** for drugs that can't cross the blood–brain barrier
- **intravenous chemotherapy** for drugs that can cross the blood–brain barrier.

You might be given CNS prophylaxis by either or both methods. It is difficult for doctors to find out which type of CNS prophylaxis works best as secondary CNS lymphoma is uncommon.

### Intrathecal chemotherapy

Intrathecal chemotherapy is where chemotherapy is given directly into the CSF. This method avoids the blood–brain barrier so chemotherapy can reach your CNS. It also means the additional chemotherapy only affects your CNS and not the rest of your body.

The chemotherapy is usually injected during a **lumbar puncture**.

Only certain drugs can be safely given intrathecally (into the CSF). The most common drug given intrathecally for CNS prophylaxis is methotrexate. For CNS prophylaxis, intrathecal methotrexate is usually given once during each cycle of standard chemotherapy.

You are likely to have fewer **side effects** if drugs are given intrathecally than if they are given intravenously. Side effects might include:

- **nausea and vomiting**
- headache (this is common after a **lumbar puncture**)  
- fever.

Rarely, more serious side effects can occur if CSF leaks from the injection site or if there is any damage to your CNS during or following the procedure.

[Cancer Research UK](https://www.cancerresearchuk.org/) have more information on methotrexate, including information on side effects.
Intravenous chemotherapy

Certain drugs can cross the blood-brain barrier when given intravenously (into a vein). The most common drug given intravenously as CNS prophylaxis is high-dose methotrexate.

Intravenous methotrexate for CNS prophylaxis is given as an infusion (drip). It typically takes 3 to 4 hours for the drug to be given. You have to stay in hospital for a few days as you need to have lots of fluids before and after the drug is given. This reduces the risk of side effects. Common side effects include:

- Problems due to too much fluid circulating in your body. This can cause breathlessness and swelling.
- Problems with kidney function. This is usually temporary and recovers but occasionally, serious problems can develop, which can be ongoing.
- Problems with liver function. This is usually temporary and recovers but very rarely, serious problems can develop.

Other intravenous drugs that can be used as CNS prophylaxis include cytarabine and ifosfamide. These drugs are both included in the standard treatment for Burkitt lymphoma. The intensive regimens used for Burkitt lymphoma are sometimes used for people with DLBCL when doctors think it might not respond well to the usual treatment, R-CHOP. Cytarabine is used as part of the standard treatment for people with mantle cell lymphoma who are fit enough for intensive treatment.

Your medical team should explain to you which side effects you can expect depending on the drugs you are having and your individual circumstances.

More detailed information on side effects for each drug is available at the electronic Medicines Compendium (eMC).

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 or phone on 01296 619409 if you would like a copy.
Further reading

- Types of lymphoma
- CNS lymphoma
- Chemotherapy
- Chemotherapy regimens
- Side effects of lymphoma treatment
- Late effects of lymphoma treatment
- Glossary
Acknowledgements

- We would like to thank the Expert Reviewers and members of our Reader Panel who gave their time to review this information.

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