

Rituximab for lymphoma

This information is about rituximab, an antibody therapy used in the treatment of certain types of lymphoma.

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Although rituximab can be used to treat other diseases such as rheumatoid arthritis, this information is only about its use in treating lymphoma.

We have separate information about the topics in **bold font**. Please get in touch if you'd like to request copies or if you would like further information about any aspect of lymphoma. Phone 0808 808 5555 or email information@lymphoma-action.org.uk.

What is rituximab?

Rituximab was the first **antibody therapy** used in the treatment of lymphoma. It was designed to bind (stick) to an antigen, a protein on the surface of a cell, called 'CD20'. CD20 is found on the surface of specialised white blood cells called **B lymphocytes** (or B cells) that normally fight infection. Most types of **lymphoma** develop from a B cell. Rituximab is therefore used to treat many types of **B-cell lymphoma**.

Rituximab is not given to treat all types of B-cell lymphomas. The cancerous B cells need to have the CD20 protein on their surface for rituximab to be effective. This means rituximab is not given for classical Hodgkin lymphoma, as the lymphoma cells do not usually have CD20. However, rituximab is often used to treat a rare type of Hodgkin lymphoma called 'nodular lymphocyte-predominant Hodgkin lymphoma' (NLPHL), as this type of lymphoma does have CD20 on its cells.

Rituximab does not work in lymphomas that have developed from **T lymphocytes (T-cell lymphomas)**. However, the cancerous T cells in some types of T-cell lymphoma, like **angioimmunoblastic T-cell lymphoma (AITL)**, can cause abnormal numbers of B cells to be produced. In these cases, rituximab can be given.

Healthy B cells also have CD20 on their surface. This means rituximab destroys some healthy B cells that are not part of the lymphoma, too. As B cells are part of the **immune system**, you may be more likely to get infections during treatment. Your body will replace the healthy B cells when you have finished treatment with rituximab.

Several **biosimilars** to rituximab (medicines that are almost identical to rituximab but are made by different manufacturers) have been approved for use in Europe and are used in the UK. These are different brands of rituximab. Rituximab biosimilars are only approved for use if they are proven to work in the same way as the original rituximab, which has the brand name MabThera®.

Who can have it?

Rituximab is **approved in Europe** to treat adults with:

- **follicular lymphoma**
- **diffuse large-B cell lymphoma (DLBCL)**
- **chronic lymphocytic leukaemia (CLL).**

It is also widely used to treat other types of **B-cell non-Hodgkin lymphoma** and **nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)**.

Rituximab is approved, in combination with chemotherapy, to treat children 6 months and over with advanced stage DLBCL, **Burkitt lymphoma** or Burkitt-like lymphoma.

Is it available on the NHS in the UK?

Rituximab is widely available on the NHS throughout the UK to treat B-cell non-Hodgkin lymphomas, in addition to CLL and NLPHL.

Benefits

Rituximab works in many types of lymphoma, either alone or combined with **chemotherapy**. It is most often given together with chemotherapy as a chemo-immunotherapy **regimen** (combination of drugs).

If you have a B-cell non-Hodgkin lymphoma, CLL or NLPHL, you are likely to have chemo-immunotherapy as your first treatment. The choice of chemotherapy that is given with rituximab depends on what type of lymphoma you have and your individual circumstances. There are now **different antibodies** that work on the same target as rituximab – a protein called CD20 – and some people have those as part of their chemo-immunotherapy regimen instead of rituximab.

Rituximab usually causes fewer **side effects** than chemotherapy, so it is sometimes used on its own for people who are not well enough to be treated with chemotherapy.

Some people with **advanced-stage follicular lymphoma** that is not yet causing problems might be offered a short course of rituximab to delay the need for more treatment.

In some types of lymphoma, such as **follicular lymphoma** and **mantle cell lymphoma**, rituximab is also used as **maintenance therapy** after chemotherapy has been completed. For maintenance, rituximab is given on its own once every 2 to 3 months, usually for around 2 years. Maintenance therapy helps to keep the disease in **remission** (no evidence of lymphoma) by targeting and killing lymphoma cells left over after chemotherapy.

Some of the benefits of rituximab seen in clinical trials include the following:

- **Adding rituximab to chemotherapy to treat some types of high-grade lymphoma increases the chance of cure and prolongs life expectancy.** This is best demonstrated for DLBCL, where the addition of rituximab to chemotherapy has enabled many more patients to be cured of their lymphoma and live longer than they would have done without it.
- **Adding rituximab to chemotherapy to treat several types of lymphoma increases the length of remissions.** Studies in follicular lymphoma, for example, have shown that people who had rituximab added to their chemotherapy lived for around three times longer without their lymphoma getting worse than those who had chemotherapy alone. In CLL, people treated with rituximab and chemotherapy had several more months of remission before they needed more treatment compared with those treated with chemotherapy alone.
- **People who do not respond to other treatments might respond to rituximab.** In a study of people with follicular lymphoma who had not responded to previous treatment, around half had a reduction in their lymphoma when rituximab was given on its own.

- **Having maintenance rituximab for follicular lymphoma can reduce the risk of the lymphoma coming back by half.** Maintenance hasn't been shown to increase the time people live, but it means they might have a longer period before they need more treatment. Some people might never need more treatment.
- **Maintenance therapy for mantle cell lymphoma increases the time people live overall and increases the time they stay in remission.** Maintenance is usually given after initial treatment and a **stem cell transplant**, but might also be given after initial treatment to people who are not able to have a stem cell transplant.
- **A short course of rituximab for advanced-stage follicular lymphoma without troublesome symptoms might delay the need for more treatment.** Fewer people given a short course of rituximab need treatment after 3 years than those who had no treatment initially. Some people might never need more treatment for their lymphoma.

If your lymphoma comes back or doesn't respond to your first treatment, you might have further treatment that includes rituximab, for example it might be given with a different chemotherapy regimen.

How is it given?

Rituximab is usually given in a day-care unit. If you are having rituximab together with **chemotherapy**, it is usually given just before the chemotherapy drugs on the first day of each cycle. Rituximab can also be given on its own for some **types of lymphoma** and for some people who are not able to have chemotherapy at all.

Rituximab can also be given as a short course of treatment for follicular lymphoma to delay the need for further treatment. In these cases, rituximab is usually given once a week for 4 weeks.

Rituximab is usually given as an intravenous infusion (through a vein). Depending on your type of lymphoma, it may be given by subcutaneous injection (injection into the layer of fat just beneath the skin). You can only be given subcutaneous rituximab if you have received at least one full dose by intravenous infusion over the course of 1 day.

Intravenous infusion

The first infusion is given slowly, over 4 to 5 hours. Remaining doses can be given more quickly – over about an hour – if you have not had a bad reaction previously.

Your dose depends on the type of lymphoma you have. For some types of lymphoma, the dose is calculated based on your weight.

Subcutaneous injection

The rituximab subcutaneous injection was approved in Europe in 2014 for use in people with follicular lymphoma and DLBCL. This method may not be available at every centre and in England, the NHS only funds subcutaneous rituximab for maintenance treatment. Only certain brands of rituximab can be given by subcutaneous injection.

When given by subcutaneous injection, rituximab is injected slowly over about 5 minutes into the abdomen (tummy).

In clinical trials, the subcutaneous injection was just as effective as the intravenous infusion.

The same dose of rituximab is usually recommended for everyone treated by subcutaneous injection, regardless of body weight.

Possible side effects

All medicines can cause **side effects** (unwanted effects of treatment). Only the most common side effects are described on this page. Your medical team should discuss the most up-to-date information with you. Read all the information you are given about rituximab, which will tell you more about possible side effects. The best time to ask any questions you might have about possible side effects is before you start treatment.

You also need to tell your medical team about any other conditions you have and any medicines, supplements or complementary therapies you are taking before you start any new treatment.

Your medical team monitor you closely for side effects during treatment. They can tell you what to look out for and who to contact if you have any problems.

Rituximab generally doesn't cause many side effects because it targets only B cells. Some people will not have any side effects. Tell your medical team if you develop any new problems during or after rituximab treatment.

The most common side effects happen in the first 2 hours of the first infusion and are known as 'infusion-related' side effects. These include fever, chills and shivering. Although they are usually called 'infusion-related', the same side effects can happen with subcutaneous rituximab, not just the intravenous form.

Most people (nearly 8 in every 10 people) have some infusion-related side effects with their first dose. The first dose of rituximab is always given as an infusion so your reaction can be monitored and the infusion stopped or slowed down if necessary. You can only have subcutaneous rituximab if you didn't have a bad reaction to the intravenous form, because the subcutaneous form can't be stopped mid-treatment if you have a bad reaction. Infusion-related side effects are less likely to happen with later doses. The number of people with infusion-related side effects drops to below 1 in 100 people after eight doses of rituximab.

To help prevent side effects developing, you should be given medicines before your treatment starts. These include paracetamol and an antihistamine, but you might be given other medicines as well. You are closely monitored during your treatment, with your temperature, pulse and blood pressure being checked regularly. If you think you are having any side effects, tell your nurse straightaway.

The other most common side effects of rituximab, which can affect more than 1 in 10 people, are:

- infections, including bacterial infections and viral infections
- bronchitis (inflammation of the airways in the lungs), which might cause symptoms like a cough
- effects on the blood: leucopenia (low levels of white blood cells), including **neutropenia** (low levels of neutrophils, a type of white blood cell), febrile neutropenia (neutropenia with a fever) and **thrombocytopenia** (low platelets)
- swelling beneath the skin
- **nausea**
- **skin rash, itching**
- **hair loss**
- a feeling of weakness
- headache
- low antibody levels.

If you have troublesome side effects, rituximab may be stopped or the infusion slowed down for a while. Once the effects have eased off, it will be slowly restarted, and you will be carefully monitored.

Other severe side effects

Severe side effects with rituximab are very uncommon but other side effects that could be severe include:

- severe infusion-related reactions
- increased risk of infection
- other low blood counts.

Severe infusion-related reactions

A small number of people who are given rituximab have a more severe infusion-related reaction, which could be:

- **Cytokine release syndrome:** Cytokines are small proteins that are important in cell signalling. Rituximab can cause a lot of cytokines to be released at once, causing an inflammatory response throughout your whole body. You might have fever, chills, swelling and difficulty breathing, which usually start between 30 minutes and 2 hours after treatment begins.
- **Tumour lysis syndrome:** When rituximab kills cancer cells, they release chemicals as they break down. If a lot of cells break down at once, this can cause problems for your kidneys. Tumour lysis syndrome is rare. It is more likely to occur when you have a lot of lymphoma in your body or a large number of cancerous cells circulating in your blood. It is most likely to happen in people with CLL. If your doctor thinks you could be affected, you might be given medication to prevent this before treatment. Rituximab might also be administered more slowly than usual or over 2 days. You will be monitored carefully.
- **Anaphylactic allergic or hypersensitivity reaction:** Some people have allergic reactions to rituximab or one of the components of the drug solution. These tend to happen within a few minutes of the drug being started. Symptoms are similar to those for cytokine release syndrome.

If you have any of these reactions, treatment will be stopped straightaway. You will be given drugs to treat the symptoms and lessen the reaction, but you might need to stay in hospital to be monitored to make sure you are recovering well. Sometimes the drug can be carefully restarted when you have recovered.

Increased risk of infection

Rituximab, especially if given with chemotherapy, can lower the number of specialised white blood cells (neutrophils) available to fight infections. When you don't have enough neutrophils, you have **neutropenia**. As it targets B cells, rituximab can also damage healthy B cells that are part of your body's defence against infection.

Until your white blood cell counts recover, you have a higher chance of getting an infection. You should tell your medical team immediately if you develop any **sign of infection**, such as a temperature, cough, diarrhoea, pain when passing urine, or if you feel generally unwell.

A very small number of people receiving rituximab develop a viral brain infection known as progressive multifocal leukoencephalopathy (PML). This is a serious complication but fortunately it is very rare.

Other low blood counts

Red blood cell and platelet counts can drop after treatment with rituximab, especially if you are having chemotherapy too. A lack of red blood cells (**anaemia**) can make you feel tired and short of breath. A lack of platelets (**thrombocytopenia**) makes you more likely to bleed or bruise easily.

Are there any side effects with rituximab by subcutaneous injection?

The same side effects occur with subcutaneous rituximab as with intravenous rituximab. However, if you are treated with subcutaneous rituximab you might have a reaction around the area where you had the injection. This can include pain, swelling and rash. These normally go away without treatment.

Precautions

Your doctor may reduce your dose and monitor you more closely or recommend that you do not take rituximab if you have certain other conditions. For example, people who have had certain infections in the past, such as hepatitis B, need to be monitored carefully to make sure the infection doesn't flare up during treatment with rituximab.

Make sure you tell your doctor about any medical conditions and any medicines you are taking.

Your doctor might also change your dose if you experience troublesome side effects.

Rituximab is not recommended for pregnant or breastfeeding women. Women should use effective contraception to prevent pregnancy during treatment and for 12 months afterwards. **If you are pregnant** and need treatment, your doctor will discuss the risks and benefits of all the possible treatments with you. There is no evidence that rituximab affects your fertility. Do not breastfeed if you are being treated with rituximab or for 12 months after your treatment has finished.

You should not be immunised with live **vaccines** while you are receiving treatment with an antibody or for at least 6 months afterwards. Some doctors recommend that you avoid live vaccines for longer so it is important to discuss this with your doctor.

Live vaccines are given for rubella, mumps and measles (often given together as the MMR), shingles, tuberculosis and yellow fever. The nasal spray flu vaccine is also a live vaccine, but the injection is not. You can still have other non-live vaccines, such as the winter flu jab. However, these might not be as effective as usual.

Research has shown that immunisations you had in the past, such as MMR, should still be effective after treatment with rituximab.

References

The full list of references for this page is available on our website. Alternatively, email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

Acknowledgements

- With thanks to Dr Graham Collins, consultant haematologist, Oxford, for reviewing this information. Dr Graham Collins has received honoraria from Roche for speaker and consultancy fees.
 - We would like to thank the members of our Reader Panel who gave their time to review this information.
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Content last reviewed: February 2019

Updated: February 2020

Next planned review: February 2022

LYMweb0196Rituximab2019v3



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