

## Ibrutinib

This information is about ibrutinib, a targeted drug used in the treatment of certain types of lymphoma.

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## What is ibrutinib?

Many newer [treatments for lymphoma](#) are [targeted drugs](#).

Targeted drugs aim to kill the type of cell that has turned **cancerous** or stop signals that make cancerous cells grow or divide. In lymphoma, the type of cell that becomes cancerous is called a 'lymphocyte' (a type of white blood cell that fights infection). There are several types of lymphocyte that can become cancerous. Ibrutinib targets B lymphocytes (B cells) and is therefore used to treat **B-cell lymphomas**.

Cells send and receive signals to other cells. Some of these signals keep cells alive and make them divide. There are lots of signalling pathways and signals are sent along one or more of these pathways. Ibrutinib (Imbruvica<sup>®</sup>) is a **cell signal blocker** that targets a protein called 'Bruton's tyrosine kinase' (BTK). BTK is a part of a pathway that helps B cells to stay alive and divide. Blocking BTK can make B cells die or prevent them dividing. This treatment can therefore stop the spread of cancerous B cells.

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## Who can have it?

Ibrutinib is **approved in Europe** for treating three types of lymphoma.

### Mantle cell lymphoma

- For people whose lymphoma has **relapsed** (come back) or has not responded to treatment (**refractory lymphoma**). Ibrutinib is given on its own.

### Chronic lymphocytic leukaemia (CLL)

- For people who have not yet had treatment for their CLL (first-line treatment). Ibrutinib can be given on its own or in combination with **rituximab** or **obinutuzumab** (**antibody therapies**).
- For people whose CLL has relapsed after treatment. For people with relapsed CLL, ibrutinib can be given on its own or with bendamustine (a **chemotherapy** drug) and **rituximab**.

### Waldenström's macroglobulinaemia (WM)

- For people who have previously received other treatments for WM. Ibrutinib is given on its own.
- For people who can't have chemo-immunotherapy (**chemotherapy** with **antibody therapy**) as first-line treatment. Ibrutinib is given on its own.

European approval to use ibrutinib in CLL and mantle cell lymphoma was granted in November 2014. It was then extended to WM in May 2015. In 2016, the European Medicines Agency (EMA) expanded ibrutinib's recommended uses for CLL.

Ibrutinib is being tested in further clinical trials in people with these types of lymphoma. This is to see if ibrutinib could work better in combination with other treatments, such as chemotherapy or antibody therapy (for example, rituximab). It is also being tested in other **types of lymphoma**. Use our searchable database to see if there's a clinical trial that might be suitable for you at **Lymphoma TrialsLink**.

## Is it available on the NHS in the UK?

Ibrutinib has been **assessed by health authorities** for some uses on the NHS in the UK. It is currently only available on the NHS for some people in certain parts of the UK.

## In Scotland

- For people with relapsed or refractory **mantle cell lymphoma**.
- For **people with relapsed or refractory CLL** who can't have treatments that include fludarabine.
- For **people with CLL and a 17p deletion** (a genetic change that means the CLL does not respond well to chemo-immunotherapy).

## In England and Wales

- For people with relapsed or refractory **mantle cell lymphoma** who have only had one previous course of treatment.
- For **people with CLL** who have had previous treatment or who have a **17p deletion or TP53 mutation** (genetic changes that mean the CLL does not respond well to chemo-immunotherapy).
- Through the **Cancer Drugs Fund** for people with relapsed or refractory WM.

Ibrutinib is also being assessed by the National Institute for Health and Care Excellence (NICE) for other uses, for example in combination with different treatments for certain types of lymphoma.

Northern Ireland usually follows NICE recommendations.

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## Benefits

Ibrutinib is considered by many experts to be a 'breakthrough treatment' for some types of lymphoma. It gives higher response rates compared with other therapies for the same types of lymphoma. The main trials that led to approval of ibrutinib are briefly described below.

### Benefits in mantle cell lymphoma

Mantle cell lymphoma that has relapsed or not responded to first-line therapy can be difficult to treat. However, the main study in this area showed that more than two-thirds of 111 people treated with ibrutinib responded to the treatment (their lymphoma shrank or disappeared).

A second study in 280 people compared ibrutinib with another cancer drug, temsirolimus, in people with relapsed or refractory mantle cell lymphoma. People lived for an average of 15 months without their lymphoma getting worse when treated with ibrutinib compared with an average of 6 months when treated with temsirolimus.

## **Benefits in chronic lymphocytic leukaemia (CLL)**

Long-lasting responses have been seen in people with CLL treated with ibrutinib. In the main trial involving 391 people with relapsed or refractory CLL, ibrutinib was compared with **ofatumumab**, which is often used for people with CLL that has come back. One year after starting treatment, around 66 in 100 people taking ibrutinib had CLL that had stayed under control (this is called 'progression-free survival') compared with around 6 in 100 people treated with ofatumumab.

In a second study involving 269 people who hadn't yet received any treatment for their CLL, ibrutinib was compared with the chemotherapy drug chlorambucil. After 1.5 years of treatment, around 90 in 100 people taking ibrutinib had CLL that had stayed under control compared with around 52 in 100 people treated with chlorambucil.

Adding ibrutinib to bendamustine and rituximab for people with relapsed or refractory CLL was also effective in a study involving 578 people. The risk of CLL progressing was reduced by taking ibrutinib instead of a placebo (dummy treatment).

## **Benefits in Waldenström's macroglobulinaemia (WM)**

A high response rate has also been seen in people with WM – about 9 in 10 people with WM responded to ibrutinib treatment in a trial in 63 people. This trial was a significant breakthrough for WM as it is an uncommon form of lymphoma and it is therefore difficult to recruit enough people to take part in a clinical trial. This trial led to the approval of ibrutinib for WM in Europe.

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## **How is it given?**

Ibrutinib is given as tablets that are taken orally (by mouth). Your recommended dose is based on the type of lymphoma you have and your general health. Always follow the advice of your medical team when taking ibrutinib.

You have one tablet once a day. The tablets are available in different doses. The packs and tablets are colour-coded to make it easier to check what dose you are having.

- Swallow the tablets whole with a glass of water.
- Do not break or chew the tablets.
- Take the tablet at about the same time every day.
- Check the information you are given to find out what you should do if you miss a dose.

## When is ibrutinib given?

Ibrutinib is taken once daily. It can be taken every day until your lymphoma stops responding unless side effects are bad enough to make you stop treatment. You might be treated with ibrutinib for years.

Keep taking ibrutinib for as long as your medical team tells you to, even if you feel well. If ibrutinib is keeping your lymphoma under control, the lymphoma could get worse if you stop taking the drug.

## Will I need any special tests while I am taking ibrutinib?

You will need to have **blood tests** to check your health, for example your blood cell counts, while you are taking ibrutinib. Your medical team might want you to have other tests depending on any other conditions you have or any side effects you develop. For example, you might have an electrocardiogram (ECG; a heart function test that records the rhythm and electrical activity of the heart) to check how well your heart is working. How often you need these tests depends on your individual circumstances such as other health conditions you have and how your lymphoma is responding.

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## Possible side effects

All medicines can cause **side effects** (unwanted effects of treatment).

Only the most common side effects of ibrutinib are described on this page. This is not a complete list of side effects that have been reported. As ibrutinib is a new treatment, more information about possible side effects is still being gathered. There is limited information about **late effects** (side effects that only develop months or years after treatment has finished) of ibrutinib. Your team should discuss the most up-to-date information with you before you start treatment. Ask all the questions you have. Discuss with your medical team how ibrutinib might affect any other medical conditions you have. You also need to tell your medical team about any medicines, supplements or complementary therapies you are taking before you start any new treatment.

Most side effects experienced by people treated with ibrutinib are mild. In clinical studies, few people (about 5 in 100) had to reduce their dose of ibrutinib because of side effects. A similar number (about 5 in 100) had to stop treatment for this reason. Some side effects, such as diarrhoea, tend to occur early in treatment and then settle down if you continue to take ibrutinib, without needing to reduce your dose.

The most common side effects of ibrutinib, which can affect more than 1 in 5 people, are:

- **neutropenia** (low neutrophils), which increases your risk of infection
- gastrointestinal effects: **nausea**, **diarrhoea**
- musculoskeletal pain (pain in muscles and bones)
- bruising and bleeding
- rash
- fever.

Some of these risks are described in more detail below.

Although minor bleeding problems (for example bruising) are common, more serious events (for example a haemorrhage) can occur less commonly. Changes in heart rhythm can also present. These effects are described below.

## Effects on blood

Ibrutinib can decrease the number of different types of cells in your blood. These effects are usually mild but can result in an increased risk of bleeding and developing infections. Ibrutinib can also cause a temporary increase in the number of lymphocytes (a type of white blood cell) in your blood. This does not normally cause any problems. Your medical team will check your **blood cell counts** regularly.

## Bleeding problems

Ibrutinib can cause bleeding problems. These can be minor, such as bruising more easily, or serious, such as a haemorrhage. Bleeding problems could be caused by the effects of ibrutinib on platelet function. **Platelets** are found in your blood and help it to clot. It is not known why some people develop bleeding problems while others do not. People who take other drugs that affect platelets or drugs that thin the blood (anticoagulants such as warfarin) might not be able to take ibrutinib or may be monitored more carefully.

Tell your medical team if you notice any symptoms of bleeding problems so that you can receive prompt treatment: bloody or black stools (they look like tar), pink or brown urine, unexpected bleeding or bleeding that is severe or that you cannot control, vomiting blood or vomit that looks like coffee grounds, coughing up blood or blood clots, increased bruising, feeling dizzy or weak, confusion, changes in your speech, or a long-lasting headache. Your medical team might need to adjust your dose of ibrutinib or stop treatment if you experience significant bleeding problems.

## Infections

Treatment with ibrutinib can lower your number of neutrophils (a type of white blood cell that fights infection). If you have **neutropenia (low neutrophils)**, you may be at higher risk of getting an infection. Neutropenia experienced with ibrutinib is generally mild. People treated with ibrutinib commonly get

infections including colds, sore throats and sinus infections. More serious infections, for example pneumonia, can occur.

It is also possible for infections that usually remain dormant in your body to flare up during treatment with ibrutinib. You might need extra monitoring if you have ever had hepatitis B (a liver infection).

## **Heart problems**

Some people treated with ibrutinib develop heart rhythm problems. These are more likely in people who are at a higher risk of heart problems or who have had them in the past. In many cases, changes in heart rhythm are mild so you can continue taking ibrutinib but you may need to be monitored more carefully. Tell your medical team immediately if:

- you feel like your heart is beating quickly and irregularly
- you are light-headed, dizzy or faint
- you have shortness of breath or any discomfort in your chest.

Your medical team will consider carefully whether ibrutinib is suitable for you if you already have heart rhythm problems or a relevant family history.

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## **Who can't have ibrutinib?**

Some people will not be able to have ibrutinib because they are taking other medications or have other conditions. Make sure you tell your medical team about any medical conditions and any medicines you are taking. Your medical team may reduce your dose and monitor you more closely or recommend that you do not take ibrutinib if you have other conditions. These include liver problems, severe kidney problems or severe heart disease.

Some medications, including herbal remedies, can interact with ibrutinib and should not be taken with it. They could increase the risk of side effects or change the effect of ibrutinib. Give your medical team a list of all the medications you are taking. Make sure you include any vitamins, supplements or herbal remedies.

**Drugs that affect blood clotting:** At the moment, it is not recommended that ibrutinib is given with warfarin. Ibrutinib can be given with some other medicines that thin your blood or stop it from clotting but you will need to be monitored carefully because of an increased risk of bleeding. If you are taking warfarin, your medical team is likely to recommend that you change to a different blood-thinning medicine if you need to take ibrutinib. You shouldn't take certain vitamins and supplements, such as fish oil or vitamin E.

**Drugs that affect an enzyme called CYP3A4:** CYP3A4 acts on many drugs to help remove them from the body, including ibrutinib. If you are taking a drug that interferes with the action of CYP3A4, it can decrease or increase the action of ibrutinib, depending on how the drugs work together. It is important that your medical team knows about all the medications you are taking as there is a range of drugs that can have this effect, including some antibiotics and herbal remedies such as St John's Wort (used for depression and anxiety).

If you are about to have or have recently had surgery, you will not be able to take ibrutinib for at least 3 to 7 days before and after your operation, depending on the type of surgery recommended and your risk of bleeding.

Ibrutinib has not been approved for use in people under 18. You must not take ibrutinib if you are pregnant or become pregnant as it could damage your unborn baby. Discuss your treatment options with your medical team if you think you might be pregnant.

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## Precautions

You might need to take certain precautions while being treated with ibrutinib.

Certain drugs and foods can increase your risk of **side effects** during treatment with ibrutinib.

- Tell your medical team if you are taking or would like to start taking any medications including, but not limited to, vitamins, supplements and herbal remedies.
- Don't drink grapefruit juice or eat grapefruit or Seville oranges (including if it is used in marmalade). These can increase the amounts of ibrutinib in your blood.

**Report any side effects to your medical team as soon as possible. Your team might be able to give you medicine or advice to help with troublesome side effects.**

- Follow your medical team's advice if you have low blood counts.
- Do not drive or operate any machinery if you have side effects such as **fatigue** or dizziness.
- Drink plenty of fluids. **Diarrhoea** is common in people taking ibrutinib but usually goes away after a couple of days. Tell your medical team if your diarrhoea does not go away in a couple of weeks.

Ibrutinib could damage an unborn baby or be passed to your baby in breast milk. Below are some recommendations you should follow.

- Prevent getting pregnant during treatment and for at least 3 months afterwards.
- Use a barrier method of contraception, such as condoms. The effect of ibrutinib on hormonal contraceptives, for example the pill, is unknown.
- Do not breastfeed if you are taking ibrutinib.

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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](mailto:information@lymphoma-action.org.uk).

## References

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

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