



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Imbruvica (*ibrutinib*)

An overview of Imbruvica and why it is authorised in the EU

### What is Imbruvica and what is it used for?

Imbruvica is a medicine for treating adult patients with the following blood cancers:

- mantle cell lymphoma (MCL) in patients whose disease does not respond to or has come back after previous treatment;
- chronic lymphocytic leukaemia (CLL) in both previously treated and untreated patients;
- Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma).

For the treatment of MCL, Imbruvica is taken on its own. For CLL, Imbruvica can be taken on its own but can also be taken with bendamustine and rituximab, or with either obinutuzumab, rituximab or venetoclax. For patients with Waldenström's macroglobulinaemia, Imbruvica is taken on its own or with rituximab.

Imbruvica contains the active substance ibrutinib.

### How is Imbruvica used?

Imbruvica can only be obtained with a prescription, and treatment should be started and supervised by a doctor experienced in using cancer medicines.

Imbruvica is available as capsules (140 mg) and tablets (140, 280, 420 and 560 mg). For patients with mantle cell lymphoma the dose is 560 mg once a day, and for patients with CLL or Waldenström's macroglobulinaemia the usual dose of Imbruvica is 420 mg once a day. When used with venetoclax in patients with CLL, Imbruvica is given on its own for three cycles (1 cycle lasts 28 days), followed by 12 cycles of Imbruvica plus venetoclax.

Treatment with Imbruvica should continue for as long as the disease improves or remains stable and the side effects are tolerable.

If the patient is taking other medicines that may interact with Imbruvica or gets severe side effects, the doctor may lower the dose or interrupt treatment. For more information about using Imbruvica, see the package leaflet or contact your doctor or pharmacist.

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## **How does Imbruvica work?**

The active substance in Imbruvica, ibrutinib, works against cancerous B lymphocytes, a type of white blood cells. It does this by blocking an enzyme called Bruton's tyrosine kinase (Btk), which promotes survival of B lymphocytes and their migration to the organs where these cells normally divide. By blocking Btk, ibrutinib decreases survival and migration of B lymphocytes, thereby delaying progression of the cancer.

## **What benefits of Imbruvica have been shown in studies?**

### **Chronic lymphocytic leukaemia**

In one study in 391 patients whose disease did not respond to or had come back after previous treatment, 66% of patients receiving Imbruvica were still alive after one year with their disease not having progressed compared with around 6% of patients receiving another cancer medicine, ofatumumab.

In a study involving 269 patients who had not been treated before, around 90% of patients receiving Imbruvica were still alive with their disease not having progressed after 1.5 years of treatment compared with around 52% of patients receiving a cancer medicine called chlorambucil.

In a study in 578 patients whose disease had not responded to or had come back after previous treatment, death or signs that the cancer was progressing occurred in 19% of patients who took Imbruvica together with the cancer medicines bendamustine and rituximab compared with 63% in those who took bendamustine and rituximab without Imbruvica.

In a study in 229 previously untreated patients, after 31 months, 79% of patients treated with Imbruvica and obinutuzumab were alive with their disease not having progressed compared with 36% of patients who took chlorambucil and obinutuzumab.

In another study of 529 previously untreated patients, after 3 years around 12% treated with Imbruvica and rituximab had a worsening of their disease or died compared with 25% of patients treated with chemotherapy plus rituximab.

In a study involving 211 previously untreated patients, after 28 months, death or signs that the cancer was progressing occurred in 21% of patients who took Imbruvica with venetoclax compared with 64% of patients who took chlorambucil and obinutuzumab.

Another study involving 159 previously untreated patients showed that 55% of patients treated with Imbruvica plus venetoclax had a complete response (i.e. disappearance of all signs of cancer).

### **Mantle cell lymphoma**

In a study in 111 patients with mantle cell lymphoma that did not respond to or had come back after previous treatment, 21% of patients taking Imbruvica had complete response and 47% had partial response (i.e. the patient improved but some signs of the disease remained). The average duration of response to treatment was 17.5 months.

A second study in 280 such patients compared Imbruvica with another cancer medicine, temsirolimus. The average time before patients died or the disease got worse was 15 months with Imbruvica versus 6 months with temsirolimus.

## **Waldenström's macroglobulinaemia**

In one main study involving 63 patients who had previously received another treatment for Waldenström's macroglobulinaemia, the disease responded to treatment with Imbruvica in 87% of patients. Response to treatment was measured as a reduction in the blood levels of the protein IgM, which is present in high levels in patients with Waldenström's disease.

In a study involving 150 patients with Waldenström's macroglobulinaemia, after 26 months, death or signs that the cancer was progressing occurred in 19% of patients who took Imbruvica together with rituximab compared with 56% of patients who took only rituximab.

## **What are the risks associated with Imbruvica?**

The most common side effects with Imbruvica (which may affect more than 1 in 5 people) are diarrhoea, neutropenia (low levels of neutrophils, a type of white blood cell), pain in muscles and bones, haemorrhage (bleeding), rash, nausea (feeling sick), joint pain, nose and throat infections, and thrombocytopenia (low blood platelet counts).

The most serious side effects (which may affect more than 1 in 20 people) are neutropenia, thrombocytopenia, lymphocytosis (high levels of white blood cells known as lymphocytes), high blood pressure and pneumonia (lung infection). For the full list of side effects of Imbruvica, see the package leaflet.

St. John's wort (a herbal remedy used for depression and anxiety) must not be used in patients treated with Imbruvica. For the full list of restrictions, see the package leaflet.

## **Why is Imbruvica authorised in the EU?**

Imbruvica was shown to be effective at delaying progression of chronic lymphocytic leukaemia, both in untreated patients and in those who had received treatment previously. In addition, Imbruvica was effective in patients with mantle cell lymphoma that did not respond to or had come back after previous treatment, a group of patients with poor prognosis and few other treatment options. In addition, Imbruvica was shown to be effective in patients with Waldenström's macroglobulinaemia. The side effects of the medicine were considered acceptable.

The European Medicines Agency decided that Imbruvica's benefits are greater than its risks and it can be authorised for use in the EU.

## **What measures are being taken to ensure the safe and effective use of Imbruvica?**

The company that markets Imbruvica needs to provide further data on the benefits of Imbruvica in the treatment of chronic lymphocytic leukaemia from follow-up of previously treated patients.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Imbruvica have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Imbruvica are continuously monitored. Side effects reported with Imbruvica are carefully evaluated and any necessary action taken to protect patients.

## **Other information about Imbruvica**

Imbruvica received a marketing authorisation valid throughout the EU on 21 October 2014.

Further information on Imbruvica can be found on the Agency's website:

[ema.europa.eu/en/medicines/human/EPAR/imbruvica](https://ema.europa.eu/en/medicines/human/EPAR/imbruvica)

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