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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:

- chronic lymphocytic leukaemia (CLL) in previously untreated patients and in patients who have received at least one previous treatment;
- mantle cell lymphoma in patients whose disease does not respond to or has come back after previous treatment;
- Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma) in patients who have had previous treatment or who cannot have chemo immunotherapy.

Imbruvica is usually used on its ownto treat these cancers . For CLL, it can be given with two other cancer medicines, bendamustine and rituximab, in patients who have received previous treatment.

These diseases are rare, and Imbruvica was designated an 'orphan medicine' (a medicine used in rare diseases) for chronic lymphocytic leukaemia on 26 April 2012, mantle cell lymphoma on 12 March 2013 and Waldenström's macroglobulinaemia on 29 April 2014.

Further information on the orphan designations can be found on the European Medicines Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

Imbruvica contains the active substance ibrutinib.

How is Imbruvica used?

Imbruvica is available as capsules (140 mg) and tablets (140, 280, 420 and 560 mg). Patients with chronic lymphocytic leukaemia and Waldenström's macroglobulinaemia should take a dose of 420 mg once a day, whereas patients with mantle cell lymphoma should take 560 mg once a day.

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

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

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

How does Imbruvica work?

The active substance in Imbruvica, ibrutinib, works against cancerous B lymphocytes, which are a type of white blood cells affected by these diseases. 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 the 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 or had come back after previous treatment, death or signs that the cancer was progressing occurred in 19% of patients (56 of 289) who took Imbruvica together with the cancer medicines bendamustine and rituximab compared with 63% (183 of 289) in those who took bendamustine and rituximab without Imbruvica.

Mantle cell lymphoma

In a main study involving 111 patients with mantle cell lymphoma that did not respond to or had come back after previous treatment, around 68% of patients taking Imbruvica had either a complete or partial response to treatment: 21% of patients had a complete response (i.e. disappearance of all signs of cancer) and 47% had a 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 length of 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, 87% of patients responded to treatment with Imbruvica. 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.

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), musculoskeletal pain (pain in muscles and bones), haemorrhage (bleeding), bruising, rash, nausea (feeling sick) and fever. The most serious side effects are neutropenia alone or with fever, pneumonia (lung infection) and thrombocytopenia (low blood platelet counts). For the full list of all side effects reported with 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 patients previously untreated and in those who received previous treatment. 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 with poor prognosis and few other treatment options. In patients with Waldenström's macroglobulinaemia, Imbruvica was shown to be effective in previously treated patients. The safety of the medicine was 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 from the first study.

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 on 21 October 2014.

Further information on Imbruvica can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

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