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EPAR summary for the public

Imbruvica

ibrutinib

This is a summary of the European public assessment report (EPAR) for Imbruvica. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Imbruvica.

For practical information about using Imbruvica, patients should read the package leaflet or contact their doctor or pharmacist.

What is Imbruvica and what is it used for?

Imbruvica is a cancer medicine that is used to treat the following types of blood cancer that affect a type of white blood cells called B lymphocytes:

- chronic lymphocytic leukaemia. Imbruvica is used in previously untreated adults. It is also used in adults who have received previous treatment, who may be given Imbruvica on its own or with two other cancer medicines, bendamustine and rituximab;
- mantle cell lymphoma. Imbruvica is used on its own in adults whose disease does not respond to or has come back after previous treatment;
- Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma). Imbruvica is used on its own in adults who have received previous treatment for their disease, or in previously untreated patients for whom treatment with chemo-immunotherapy is not suitable.

Because the number of patients with these cancers is low, they are considered 'rare', and Imbruvica was designated an 'orphan medicine' (a medicine used in rare diseases).

Imbruvica contains the active substance ibrutinib.

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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 140 mg capsules. In chronic lymphocytic leukaemia and Waldenström's macroglobulinaemia, the recommended dose is 3 capsules once a day, whereas in mantle cell lymphoma it is 4 capsules once a day. The capsules should be taken at the same time each day and should be continued 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 dose may be lowered or treatment interrupted. A dose reduction is recommended in patients with mildly or moderately reduced liver function, whereas Imbruvica is not recommended in patients with severely reduced liver function. For more information, see the summary of product characteristics (also part of the EPAR).

How does Imbruvica work?

The active substance in Imbruvica, ibrutinib, works by blocking an enzyme called Bruton's tyrosine kinase (Btk), which is mostly found in B lymphocytes. Btk 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?

Imbruvica has been studied in 3 main studies in patients with chronic lymphocytic leukaemia. In the first study, involving 391 patients whose disease did not respond to or had come back after previous treatment, Imbruvica was more effective than ofatumumab (another cancer medicine) at delaying progression of the cancer. After 1 year of treatment, around 66% of patients receiving Imbruvica were still alive with their disease not having progressed compared with around 6% of patients receiving ofatumumab. In the second study, involving 269 patients who had not been treated before, Imbruvica was more effective than the cancer medicine chlorambucil at delaying progression of the cancer. After 1.5 years of treatment, around 90% of patients receiving Imbruvica were still alive with their disease not having progressed compared with around 52% of patients receiving chlorambucil. A third study, in 578 patients whose disease had not responded or had come back after previous treatment, compared adding Imbruvica or placebo (a dummy treatment) to the cancer medicines bendamustine and rituximab. On analysis, death or signs the cancer was progressing occurred in 19% of patients (56 of 289) who had taken Imbruvica compared with 63% (183 of 289) in those who did not get Imbruvica.

Imbruvica was also investigated in a main study involving 111 patients with mantle cell lymphoma that did not respond to or had come back after previous treatment. In this study Imbruvica was not compared with any other treatment. Results of the study showed Imbruvica to be effective, with around 68% of patients having 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 Ibrutinib versus 6 months with temsirolimus.

In Waldenström's macroglobulinaemia, Imbruvica was studied in one main study involving 63 patients who had previously received another treatment for their disease. Imbruvica was not compared with any other treatment in this study. The study showed that around 87% (55 out of 63) 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 approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Imbruvica's benefits are greater than its risks and recommended that it be approved for use in the EU.

The CHMP considered that 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 the previously treated patients, Imbruvica was also shown to be effective when combined with bendamustine and rituximab. The Committee noted that Imbruvica was also 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. Regarding Waldenström's macroglobulinaemia, Imbruvica had also a clinically relevant effect in previously treated patients, and the CHMP considered that the medicine could also benefit previously untreated patients who are unsuitable for chemo-immunotherapy and for whom no satisfactory treatments are available. In addition, the safety of the medicine was considered acceptable.

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

The company will 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.

Other information about Imbruvica

The European Commission granted a marketing authorisation valid throughout the European Union for Imbruvica on 21 October 2014.

The full EPAR and risk management plan summary for Imbruvica can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Imbruvica, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Imbruvica can be found on the Agency's website (ema.europa.eu/Find medicine/Human medicines/Rare disease designation):

- chronic lymphocytic leukaemia (26 April 2012);
- mantle cell lymphoma (12 March 2013);
- Waldenström's macroglobulinaemia (29 April 2014).

This summary was last updated in 08-2016.