27 January 2023
EMA/933469/2022
EMEA/H/C/003791/II/0073

Withdrawal of application to change the marketing authorisation for Imbruvica (ibrutinib)

Janssen-Cilag International N.V. withdrew its application for the use of Imbruvica in combination with bendamustine and rituximab for patients with previously untreated mantle cell lymphoma (MCL, a cancer of a type of white blood cell called B cells).

The company withdrew the application on 13 December 2022.

What is Imbruvica and what is it used for?

Imbruvica is a medicine used to treat certain blood cancers involving B cells:

- 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 or with other cancer medicines (bendamustine and rituximab, obinutuzumab, rituximab or venetoclax). For the treatment of Waldenström's macroglobulinaemia, Imbruvica is taken on its own or with rituximab.

Imbruvica has been authorised in the EU since October 2014. It contains the active substance ibrutinib and is available as capsules and tablets to be taken by mouth.

Further information on Imbruvica's current uses can be found on the Agency's website: ema.europa.eu/en/medicines/human/EPAR/imbruvica.

What change had the company applied for?

The company applied to extend the use of Imbruvica, in combination with bendamustine and rituximab, to treat adult patients with previously untreated MCL who cannot have an autologous stem cell transplantation (ASCT, a procedure where the patient's bone marrow is replaced by their own stem cells to form new bone marrow that produces healthy cells).

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How does Imbruvica work?

In untreated MCL, Imbruvica works in the same way as it does in its existing indications. The active substance in Imbruvica, ibrutinib, works against cancerous B cells by blocking an enzyme called Bruton's tyrosine kinase (Btk) which helps B cells survive and migrate to the organs where they normally divide. By blocking Btk, ibrutinib helps kill and reduce the number of cancer cells, thereby slowing down worsening of the cancer.

What did the company present to support its application?

The company presented the results of a study involving 523 patients who had untreated MCL and were aged 65 years or older, therefore representing a population that generally cannot have ASCT. The patients were given either Imbruvica or placebo (a dummy treatment), together with bendamustine and rituximab, and the study looked at how long they lived without their disease getting worse.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and had prepared questions for the company. After the Agency had assessed the company's responses to the questions, there were still some unresolved issues.

What did the Agency recommend at that time?

Based on the review of the information and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Imbruvica could not have been authorised for use with bendamustine and rituximab in the treatment of adults with untreated MCL who cannot have ASCT.

The agency considered that the benefits of Imbruvica in combination with bendamustine and rituximab were limited in the proposed use and had concerns about potential serious side effects with this combination, including a higher risk of serious infections. The agency also considered that it would be difficult to select patients not fit enough for ASCT, but still fit enough that the benefits of the combination would outweigh its risks. Therefore, at the time of the withdrawal, the Agency's opinion was that the benefits of Imbruvica in the treatment of patients with previously untreated MCL who are not eligible for ASCT did not outweigh its risks.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that it withdrew its application because the Agency considers that the submitted data are insufficient to support the approval for the use of Imbruvica in patients with untreated MCL who cannot have ASCT.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials using Imbruvica.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.

What is happening with Imbruvica for the treatment of other diseases?

There are no consequences on the use of Imbruvica in its authorised uses.