15 November 2024
EMA/521354/2024
EMEA/H/C/005823

Withdrawal of application to change the marketing authorisation for Inaqovi (cedazuridine and decitabine)

Otsuka Pharmaceutical Netherlands B.V. withdrew its application for the use of Inaqovi in the treatment of adult patients with myelodysplastic syndromes (conditions where the bone marrow does not make enough healthy blood cells or platelets) or chronic myelomonocytic leukaemia (another type of cancer of the white blood cells). The company withdrew the application for CMML on 5 August 2024 and for MDS on 6 November 2024.

What is Inaqovi and what is it used for?

Inaqovi is a medicine used to treat adults with newly diagnosed acute myeloid leukaemia (AML), a type of cancer affecting the white blood cells. It is used in patients who are not eligible for standard induction chemotherapy (initial treatment with cancer medicines). Inaqovi has been authorised in the EU since September 2023.

It contains the active substances cedazuridine and decitabine and is available as tablets taken by mouth.

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

What change had the company applied for?

The company applied to extend the use of Inaqovi to include the treatment of adult patients with myelodysplastic syndromes (MDS) or chronic myelomonocytic leukaemia (CMML). During the assessment the company withdrew the application for CMML and limited the indication in MDS to use in patients with MDS with a risk score of >3.5 according to the revised international prognostic scoring system (IPSS-R), which indicates a higher risk of developing a more severe form of the disease.

How does Inaqovi work?

In the treatment of MDS and CMML, Inaqovi was expected to work in the same way as it does in its existing indication.

The two active substances in Inaqovi, decitabine and cedazuridine, work in different ways. Decitabine is analogous (comparable) to cytidine, a fundamental component of the DNA (genetic material) in cells.

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In the body, decitabine is incorporated into the DNA where it blocks the activity of enzymes (proteins) called DNA methyltransferases (DNMTs). By blocking DNMTs, decitabine prevents the increase of tumour cells and leads to their death.

Cedazuridine blocks the action of an enzyme which breaks down decitabine in the gut and liver. This prevents the premature breakdown of decitabine when it is given by mouth.

What did the company present to support its application?

To support its application, the company presented the results of two studies in adults with MDS and CMML. During the first treatment cycle, patients either received Inaqovi tablets once daily for five days or decitabine by infusion (drip) into a vein once daily for five days at the beginning of a 28-day cycle. After the first cycle the treatments were reversed (i.e., the group given Inaqovi received decitabine by infusion, and vice versa). For the third and subsequent cycles, all patients were given Inaqovi.

The studies measured the proportion of patients with a complete response (few abnormal cells in the bone marrow and normal levels of blood cells in the bloodstream).

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

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared questions for the company. The company requested the withdrawal of the CMML indication and addressed the questions on MDS. After the Agency had assessed the company's responses to the last round of questions on MDS there were still some unresolved issues and the company withdrew the application for MDS.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal of the applications, the Agency had some concerns, and its provisional opinion was that Inaqovi could not have been authorised for the treatment of CMML or MDS.

The Agency had concerns relating to the clinical benefit and whether this had been sufficiently established in the proposed indication. Therefore, at the time of the withdrawal, the Agency's opinion was that the benefits of Inaqovi in the treatment of CMML or MDS 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 the application for CMML, the company stated that it did not seek to pursue the CMML indication and revised the myelodysplastic syndrome (MDS) indication to higher-risk MDS.

In its letter notifying the Agency of the withdrawal of the application for MDS, the company stated that it cannot address the major objection from the agency at this point in time.

Does this withdrawal affect patients in clinical trials?

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

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

What is happening with Inaqovi for the treatment of AML?

Inaqovi continues to be authorised in adults with newly diagnosed AML.