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Withdrawal of application to change the marketing authorisation for Gazyvaro (obinutuzumab)

Roche Registration GmbH withdrew its application for the use of Gazyvaro as a pre-treatment to reduce the risk of cytokine release syndrome (CRS) associated with Columvi (glofitamab), a cancer medicine used to treat adults with a blood cancer called diffuse large B-cell lymphoma (DLBCL).

The company withdrew the application on 4 July 2023.

What is Gazyvaro and what is it used for?

Gazyvaro is a cancer medicine used in adults to treat follicular lymphoma and chronic lymphocytic leukaemia, two types of cancer of B-lymphocytes (a type of white blood cell).

Gazyvaro has been authorised in the EU since July 2014. It contains the active substance obinutuzumab and is given as an infusion (drip) into a vein.

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

What change had the company applied for?

The company applied to extend the use of Gazyvaro as a pre-treatment to reduce the risk of CRS associated with another cancer medicine, Columvi. CRS is a potentially life-threatening overactivation of the immune system with fever, shortness of breath, low blood pressure and headache.

How does Gazyvaro work?

Columvi can cause a rapid release of cytokines (proteins that affect the immune system) leading to CRS, by attaching to white blood cells known as B cells and T cells. The active substance in Gazyvaro, obinutuzumab, is a monoclonal antibody that has been designed to attach to the protein CD20, which is found on B-cells. By attaching to CD20, obinutuzumab both lowers the level of B cells and diminishes binding of Columvi to B-cells, which would be expected to reduce the risk of CRS associated with Columvi.

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What did the company present to support its application?

The company presented the results from a study involving 154 adults given Gazyvaro 7 days before receiving Columvi for the treatment of DLBCL that had returned or was not responding after at least two other therapies. The study did not compare Gazyvaro with a placebo (dummy treatment) or other medicines. The study looked at the proportions of patients who developed CRS and severe CRS (categorised as CRS with life-threatening symptoms or symptoms requiring aggressive treatment).

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 Gazyvaro could not have been authorised for use as a pre-treatment to reduce the risk of CRS associated with Columvi.

The Agency's concerns were about the effectiveness of Gazyvaro, based on important uncertainties regarding the design and conduct of the main study. These included the lack of a comparator, the data to support the dose schedule of Gazyvaro and the impact of other medicines in reducing the risk of CRS with Columvi, including the use of corticosteroids and previous cancer medicines that reduce levels of B cells. In addition, the methods used to determine the effectiveness of Gazyvaro in reducing the risk of CRS associated with Columvi within the main study were not considered to be robust enough.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough information to support the application for a change to the marketing authorisation of Gazyvaro.

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 its decision was based on the Agency's view that the data did not allow to conclude on a positive benefit-risk balance for the use of Gazyvaro as a pre-treatment to reduce the risk of CRS associated with Columvi.

Does this withdrawal affect patients in clinical trials?

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

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

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

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