EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Questions and answers

Refusal of a change to the marketing authorisation for Arzerra (ofatumumab)

On 23 June 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of a change to the marketing authorisation for the medicinal product Arzerra. The change concerned an extension of indication to add maintenance treatment for adults with chronic lymphocytic leukaemia.

The company that applied for the change to the authorisation is Novartis Europharm Ltd. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Arzerra?

Arzerra is a cancer medicine that contains the active substance ofatumumab. It is available as a concentrate that is made up into a solution for infusion (drip) into a vein.

Arzerra has been authorised since April 2010. It is already used to treat chronic lymphocytic leukaemia (CLL), a cancer of a type of white blood cells called B lymphocytes. Arzerra is used together with chlorambucil or bendamustine (other cancer medicines) in previously untreated patients who cannot be treated with therapy using another cancer medicine, fludarabine. It can also be used in patients whose disease has not improved with treatment with fludarabine and a medicine called alemtuzumab.

What was Arzerra expected to be used for?

Arzerra was also expected to be used for maintenance treatment for adult patients with CLL whose condition has improved after at least two types of initial treatment with cancer medicines (induction therapy). The company later restricted this indication to patients at high risk of relapse.

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How is Arzerra expected to work?

In maintenance treatment for CLL, Arzerra is expected to work in the same way as it does in its existing indications. Ofatumumab, the active substance in Arzerra, is a monoclonal antibody (a type of protein) that has been designed to attach to a protein called CD20, which is present on the surface of B lymphocytes. When ofatumumab attaches to CD20, it causes the cell to die. This is expected to help control CLL by destroying the cancerous B lymphocytes.

What did the company present to support its application?

The company presented results of a clinical study that compared Arzerra with no treatment in 474 patients whose CLL had responded after at least two types of induction therapy. Among these, 142 patients were considered to be at high risk of relapse. The main measure of effectiveness was progression-free survival (how long the patients lived without their disease getting worse) but the study also looked at how long patients lived altogether (overall survival).

What were the CHMP's main concerns that led to the refusal of the change to the marketing authorisation?

The CHMP considered that there was uncertainty about the importance of the observed effect on progression-free survival associated with Arzerra. The findings on progression-free survival were not supported by other measures such as overall survival or a significant improvement in patients' quality of life.

The CHMP considered that the use of Arzerra for maintenance treatment should be seen in the context of its side effects. Common side effects of Arzerra included infusion reactions, neutropenia (low levels of neutrophils, a type of white blood cell) and upper respiratory tract infections (nose and throat infections). The CHMP considered that the data were not sufficient to conclude that maintenance treatment with Arzerra is of more benefit than no treatment.

Therefore, the CHMP was of the opinion that the benefits of Arzerra for the maintenance treatment of CLL did not outweigh its risks. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that this refusal does not have any impact on the ongoing clinical trials conducted with Arzerra. There are currently no compassionate use programmes ongoing with Arzerra.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Arzerra for of its existing uses in CLL?

There are no consequences on the use of Arzerra in its already authorised indications.

The full European Public Assessment Report for Arzerra can be found on the Agency's website ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.