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EPAR summary for the public

Zevalin

ibritumomab tiuxetan

This is a summary of the European public assessment report (EPAR) for Zevalin. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Zevalin.

What is Zevalin?

Zevalin is a kit for the preparation of a 'radiolabelled' infusion (drip into a vein) of the active substance ibritumomab tiuxetan.

What is Zevalin used for?

Zevalin is not used directly, but it must be radiolabelled before use. Radiolabelling is a technique where a substance is tagged (labelled) with a radioactive compound. Zevalin is radiolabelled by mixing it with a solution of radioactive yttrium (90Y) chloride.

- The radiolabelled medicine is used to treat adult patients with follicular B cell non Hodgkin's lymphoma. This is a cancer of the lymph tissue (part of the immune system) that affects a type of white blood cell called B lymphocytes, or B cells. Zevalin is used in the following groups of patients:
- patients who have gone into remission (reduction in the number of cancerous cells) after their first 'induction treatment' (initial chemotherapy treatment) for lymphoma. Zevalin is given as 'consolidation therapy' to improve the remission;

patients in whom rituximab (another treatment for non Hodgkin's lymphoma) is no longer effective or whose disease has come back after rituximab treatment.

The medicine can only be obtained with a prescription.

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How is Zevalin used?

Radiolabelled Zevalin treatment should only be handled and given by someone who is authorised to use radioactive medicines.

Before treatment with radiolabelled Zevalin, the patients must first receive an infusion of rituximab (at a dose lower than would be used for treatment) to clear B cells from their circulation, leaving the cancerous B cells in the lymph tissue. This enables Zevalin to deliver radiation more specifically to the cancerous B–cells. This is followed, seven to nine days later, by a second infusion of rituximab and an injection of radiolabelled Zevalin. Zevalin must be given as a slow infusion lasting 10 minutes. The dose of Zevalin is calculated to give the appropriate amount of radioactivity for the patient's condition, based on the blood cell count.

How does Zevalin work?

The active substance in Zevalin, ibritumomab, is a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and bind to a specific structure (called an antigen) that is found in certain cells in the body. Ibritumomab has been designed to target an antigen, CD20, which is present on the surface of all B lymphocytes.

When Zevalin is radiolabelled, the radioactive element yttrium 90 (90Y) is attached to ibritumomab. When the radiolabelled medicine is injected into the patient, the monoclonal antibody carries the radioactivity to the target CD20 antigen on the B cells. Once the antibody has bound to the antigen, the radiation can act locally and destroy the lymphoma B cells.

How has Zevalin been studied?

For consolidation therapy, Zevalin has been studied in one main study involving 414 patients who had achieved a partial or complete remission during induction treatment for non Hodgkin's lymphoma. The study compared patients who received Zevalin and patients who received no additional treatment. The main measure of effectiveness was the length of time the patients survived without their disease getting worse.

Zevalin has also been studied in a total of 306 patients with non Hodgkin's lymphoma who were not responding to other treatments or whose disease had come back after previous treatment. The main study compared the effectiveness of Zevalin with that of rituximab in 143 patients. In an additional study, 57 patients with follicular lymphoma who had been previously treated and were not responding to rituximab received Zevalin. In both studies, the main measure of effectiveness was the number of patients whose disease responded partially or completely to treatment.

What benefit has Zevalin shown during the studies?

When Zevalin was used as consolidation therapy, patients survived for longer without their disease getting worse than when they received no further treatment. Patients receiving radiolabelled Zevalin survived for an average of 37 months until their disease got worse, compared with 14 months in those who did not receive any further treatment. However, there were too few patients who had received rituximab as part of their induction treatment to determine whether there would be a benefit of using Zevalin as consolidation treatment in these patients.

In patients who were not responding to other treatments or whose disease had come back after previous treatment, Zevalin was more effective than rituximab: 80% of the patients receiving radiolabelled Zevalin responded, compared with 56% of the patients receiving rituximab. However, the time taken for the disease to get worse after treatment was the same in both groups (about 10

months). In the additional study, radiolabelled Zevalin brought about a response in about half of the patients.

What is the risk associated with Zevalin?

Radiolabelled Zevalin is radioactive and its use may carry a risk of cancer and hereditary defects. The doctor who prescribes it must ensure that the risks linked to the exposure to the radioactivity are lower than the risks from the disease itself. The most common side effects with Zevalin (seen in more than 1 patient in 10) are anaemia (low red blood cell counts), leucocytopenia and neutropenia (low white blood cell counts), thrombocytopenia (low blood platelet counts), asthenia (weakness), pyrexia (fever), rigors (stiffness) and nausea (feeling sick). For the full list of all side effects reported with Zevalin, see the package leaflet.

Zevalin should not be used in people who may be hypersensitive (allergic) to ibritumomab, yttrium chloride, mouse proteins or any of the other ingredients. Zevalin must not be used in patients who are pregnant or breast feeding.

Why has Zevalin been approved?

The CHMP decided that Zevalin's benefits are greater than its risks as consolidation therapy after remission induction in previously untreated patients with follicular lymphoma and for the treatment of adult patients with rituximab relapsed or refractory CD20-positive follicular B cell non Hodgkin's lymphoma. The Committee recommended that Zevalin be given marketing authorisation.

Zevalin was originally authorised under 'exceptional circumstances' because it had not been possible to obtain complete information about Zevalin. As the company had supplied the additional information requested, the 'exceptional circumstances' ended on 22 May 2008.

Other information about Zevalin

The European Commission granted a marketing authorisation valid throughout the European Union for Zevalin on 16 January 2004.

The full EPAR for Zevalin 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 Zevalin, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 09-2011.