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Ebvallo (*tabelecleucel*)

An overview of Ebvallo and why it is authorised in the EU

What is Ebvallo and what is it used for?

Ebvallo is a medicine used to treat adults and children from 2 years of age who, after receiving an organ- or a bone marrow-transplantation, develop a blood cancer called Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD).

EBV+ PTLD is a potentially fatal complication that can occur after transplantation. Following a transplant, patients receive medicines that weaken their immune system (the body's natural defences) to prevent rejection of the transplant. However, their weakened immune system makes these patients vulnerable to infection with viruses such as the Epstein-Barr virus. In patients with EBV+ PTLD, the Epstein-Barr virus infects white blood cells called B cells after transplantation, causing changes to these cells that can lead to cancer.

Ebvallo is used in patients who have received at least one previous treatment, when the disease comes back (relapsed) or when the treatment does not work (refractory).

PTLD is rare, and Ebvallo was designated as an 'orphan medicine' (a medicine used in rare diseases) on 21 March 2016. Further information on the orphan designation can be found here: www.ema.europa.eu/medicines/human/orphan-designations/eu-3-16-1627.

Ebvallo contains the active substance tabelecleucel.

How is Ebvallo used?

Ebvallo can only be obtained with a prescription and should be given under the supervision of a doctor experienced in the treatment of cancer; it should be given in a controlled setting where adequate facilities for managing side effects, including those requiring urgent interventions, are available.

Ebvallo is given by injection into a vein; the dose depends on the body weight of the patient. It is given over several 35-day cycles, during which patients receive Ebvallo on days 1, 8 and 15, and are kept under observation until day 35.

The number of cycles of Ebvallo depends on how patients respond to treatment; this is evaluated at around day 28 of each cycle.

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For more information about using Ebvallo, see the package leaflet or contact your doctor or pharmacist.

How does Ebvallo work?

The active substance in Ebvallo, tabelecleucel, is made of cells of the immune system called T cells that have been taken from a donor. The T cells are first mixed with B cells from the same donor which have been infected with the Epstein-Barr virus, so that the T cells learn to recognise infected B cells as 'foreign'. The T cells are then grown in the laboratory to increase their numbers. When the medicine is then given to the patient, the T cells attack and kill the patient's own infected B cells, helping to control EBV+ PTLD.

What benefits of Ebvallo have been shown in studies?

Ebvallo was shown to be effective at controlling EBV+ PTLD in one main study involving 43 patients who developed the disease after receiving an organ or bone marrow transplant, and in whom at least one previous treatment had failed.

In the group of patients who developed EBV+ PTLD after an organ transplant, 15 out of 29 patients achieved a complete or partial response, meaning that signs of cancer disappeared or decreased. In the group of patients who developed EBV+ PTLD after a bone marrow transplant, 7 out of 14 patients had a complete or partial response to Ebvallo. A durable response lasting longer than 6 months was observed in 4 patients from the organ transplant group, and in 6 patients from the bone marrow transplant group.

What are the risks associated with Ebvallo?

The most common side effects with Ebvallo (which may affect more than 1 in 10 people) are fever, diarrhoea, tiredness, nausea (feeling sick), anaemia (low levels of red blood cells), decreased appetite, hyponatraemia (low blood sodium levels), abdominal (belly) pain, low levels of white blood cells, including neutrophils (white blood cells that fights infections), increased blood levels of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase (signs of possible liver damage), constipation, hypoxia (low blood oxygen levels), dehydration, hypotension (low blood pressure), nasal congestion and rash.

The most serious adverse reactions, which may affect up to 1 in 10 people, are tumour flare reaction (a reaction to certain medicines that act on the immune system which is similar to worsening of the cancer; symptoms may include painful and swollen lymph nodes, enlarged spleen, slight fever, bone pain and skin rash) and graft-versus-host disease (when transplanted cells attack the body).

For the full list of side effects and restrictions of Ebvallo, see the package leaflet.

Why is Ebvallo authorised in the EU?

Ebvallo was shown to produce clinically significant responses (complete or partial) in around half of patients involved in the main study. These results are considered promising in a setting where patients generally have a very poor prognosis and limited treatment options. Warnings in the product information and other risk minimisation measures are considered adequate to manage the important safety concerns identified during the clinical studies with Ebvallo.

The European Medicines Agency therefore decided that Ebvallo’s benefits are greater than its risks and it can be authorised for use in the EU. Ebvallo has been authorised under ‘exceptional circumstances’. This is because it has not been possible to obtain complete information about Ebvallo due to the rarity

of the disease. Every year, the Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Ebvallo?

Since Ebvallo has been authorised under exceptional circumstances, the company that markets the medicine will provide the final results of the main ongoing study with Ebvallo to further characterise the long-term safety and effectiveness of the medicine; the company will also conduct a study in Europe on the safety and effectiveness of Ebvallo when used outside of clinical studies.

What measures are being taken to ensure the safe and effective use of Ebvallo?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Ebvallo have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Ebvallo are continuously monitored. Suspected side effects reported with Ebvallo are carefully evaluated and any necessary action taken to protect patients.

Other information about Ebvallo

Ebvallo received a marketing authorisation valid throughout the EU on 16 December 2022.

Further information on Ebvallo can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/ebvallo

This overview was last updated in 12-2022.