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EPAR summary for the public

Zalmoxis

Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2)

This is a summary of the European public assessment report (EPAR) for Zalmoxis. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Zalmoxis.

For practical information about using Zalmoxis, patients should read the package leaflet or contact their doctor or pharmacist.

What is Zalmoxis and what is it used for?

Zalmoxis is a medicine used as an add-on treatment in adults who have received a haematopoietic stem cell transplant (HSCT, a transplant of cells that can develop into different types of blood cells) from a partially matched donor (a so-called haploidentical transplant). Zalmoxis is used in patients who have received a haploidentical HSCT because they have serious blood cancers, such as certain leukaemias and lymphomas. Before receiving an HSCT, the patient will have received treatment to remove existing cells from the bone marrow, including cancer cells and immune cells. Zalmoxis is given to help restore the patient's immune system after the transplant.

Zalmoxis is a type of advanced therapy medicine called a 'somatic cell therapy product'. This is a type of medicine containing cells or tissues that have been manipulated so that they can be used to cure, diagnose or prevent a disease. Zalmoxis contains T cells (a type of white blood cell) that have been genetically modified[1]. To make Zalmoxis, T cells from the HSCT donor are separated from the rest of the cells in the transplant. These T cells are then genetically modified to include a 'suicide gene'.

[1] Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Because the number of patients undergoing haploidentical HSCT is low, Zalmoxis was designated an 'orphan medicine' (a medicine used in rare diseases) on 20 October 2003.

How is Zalmoxis used?

Zalmoxis can only be obtained with a prescription and treatment is given under the supervision of a doctor who has experience in the treatment of blood cancers using HSCT.

Zalmoxis is prepared for use in a specific patient. It is given 21 to 49 days after transplantation, but only if the transplant has not already restored the patient's immune system and if the patient has not developed graft-versus-host disease (when transplanted cells attack the body).

Zalmoxis is given as an infusion (drip) into a vein lasting 20 to 60 minutes, every month for up to four months until the circulating T cells reach a certain level. The dose of Zalmoxis depends on the bodyweight of the patient.

For further information, see the package leaflet.

How does Zalmoxis work?

When given after transplantation, Zalmoxis helps the patient to build up their immune system and so helps to protect them from infections. However the T cells in Zalmoxis can sometimes attack the patient's body, causing graft-versus-host disease. The T cells in Zalmoxis have a suicide gene, which makes them susceptible to the medicines ganciclovir and valganciclovir. If the patient develops graft-versus-host disease, ganciclovir or valganciclovir is given, which kills the T cells that have the suicide gene thereby treating the disease and preventing its further development.

What benefits of Zalmoxis have been shown in studies?

Zalmoxis has been investigated in a main study involving 30 patients who had haploidentical HSCT for serious blood cancers. In this study, Zalmoxis was not compared with any other treatment. The main measure of effectiveness was restoration of the immune system as measured by blood levels of T cells. 77% of the patients receiving Zalmoxis (23 out of 30) had their immune systems restored. Graft-versus-host disease occurred in 10 patients who were then given ganciclovir or valganciclovir, either alone or in combination with other medicines. All 10 patients recovered from graft-versus-host disease.

Data from the main study were also combined with data from a second ongoing study, and survival rates for 37 patients treated with Zalmoxis (23 from the main study and 14 from the ongoing study) were compared with rates from a patient database of 140 patients who have undergone haploidentical HSCT in the past. The number of patients who survived after one year was 51% for patients who received Zalmoxis compared with 34 to 40% for patients who did not receive Zalmoxis.

What are the risks associated with Zalmoxis?

The most common side effect with Zalmoxis (which may affect more than 1 in 10 people) is acute graft-versus-host disease (where the condition develops within approximately 100 days of the transplant). When using Zalmoxis, this can be treated with ganciclovir or valganciclovir.

Zalmoxis must not be used in patients whose immune system has been restored. It must also not be used in patients who have already developed graft-versus-host disease that requires treatment.

For the full list of restrictions and side effects reported with Zalmoxis, see the package leaflet.

Why is Zalmoxis approved?

Zalmoxis has been shown to help restore the immune systems of patients who had haploidentical HSCT for serious blood cancers; these patients have limited treatment options and a poor prognosis. The safety profile of Zalmoxis is considered acceptable. The main risk is graft-versus-host disease, however this can be successfully treated with ganciclovir or valganciclovir, which kill the T cells in Zalmoxis.

Although more data are needed to determine the size of the benefit, the Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Zalmoxis' benefits are greater than its risks and recommended that it be approved for use in the EU.

Zalmoxis has been given 'conditional approval'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this summary will be updated as necessary.

What information is still awaited for Zalmoxis?

Since Zalmoxis has been granted a conditional approval, the company that markets Zalmoxis will provide the results of an ongoing study in high-risk acute leukaemia patients. The study will compare haploidentical HSCT followed by treatment with Zalmoxis with haploidentical HSCT containing T cells followed by treatment with cyclophosphamide (a medicine to prevent graft-versus-host disease) and with haploidentical HSCT without T cells.

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

The company that markets Zalmoxis will provide educational material for healthcare professionals with detailed information on the risks, including graft-versus-host disease, and how to use the medicine correctly. The company will also collect data from all patients treated with Zalmoxis through a registry and will monitor their progress after treatment to study long-term safety and effectiveness of the medicine.

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

Other information about Zalmoxis

The European Commission granted a marketing authorisation valid throughout the European Union for Zalmoxis on 18 August 2016.

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

The summary of the opinion of the Committee for Orphan Medicinal Products for Zalmoxis can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 08-2016.