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Public summary of opinion on orphan designation

Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured for the treatment of acute lymphoblastic leukaemia

On 19 October 2020, orphan designation EU/3/20/2344 was granted by the European Commission to Kite Pharma EU B.V., Netherlands, for autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (also known as KTE-X19) for the treatment of acute lymphoblastic leukaemia.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia (ALL) is a cancer of certain white blood cells called lymphocytes, which multiply too quickly and live too long, so there are too many of them circulating in the blood. These lymphocytes are not fully developed and do not work properly. Over time, these abnormal cells replace the normal white cells, red cells and platelets in the bone marrow (the spongy tissue inside the large bones in the body, where blood cells are produced).

ALL is the most common type of leukaemia in young children. This disease also affects adults, especially those aged 65 and older. ALL is a serious and life-threatening condition because the abnormal immature cells take the place of the normal blood cells, reducing the patient's ability to fight infections and causing organ damage.

What is the estimated number of patients affected by the diagnosis of the condition?

At the time of designation, acute lymphoblastic leukaemia affected less than 1.4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 73,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

*For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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What treatments are available?

Treatment for leukaemia is complex and depends on a number of factors including the type of leukaemia, the extent of the disease and whether the leukaemia has been treated before. It also depends on the patient's age, symptoms, and general health. At the time of submission of the application for orphan designation, the primary treatment of ALL was chemotherapy (medicines that kill cancer cells) and stem-cell transplantation (a procedure where the patient's bone marrow is cleared of cells and replaced with stem cells that produce healthy blood cells). Treatments for patients who have been treated before included blinatumomab, inotuzumab ozogamicin and tisagenlecleucel.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALL because early studies show that it might work in patients whose disease was not controlled with other treatments or had come back. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The abnormal lymphocytes in patients with ALL produce a protein on their surface called CD19. The medicine is made up of T cells (cells of the immune system) which are taken from the patient and modified in the laboratory using a virus that carries a gene into the cells, allowing them to produce a protein called chimeric antigen receptor (CAR) that targets CD19. The modified T cells are grown in the laboratory to increase their number. When they are given back to the patient, the T cells are expected to attach to CD19 on the cancer cells and kill them.

The type of virus used in this medicine does not cause disease in humans.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with ALL were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of ALL. Orphan designation of the medicine had been granted in the United States for the treatment of ALL.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a Positive opinion on 10 September 2020, recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a

marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Contact details of the current sponsor for this orphan designation can be found on EMA website.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.