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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic T cells encoding an exogenous TK gene for the treatment of acute myeloid leukaemia

On 20 September 2010, orphan designation (EU/3/10/773) was granted by the European Commission to LTKFarma SAS, France, for allogeneic T cells encoding an exogenous TK gene for the treatment of acute myeloid leukaemia.

What is acute myeloid leukaemia?

Acute myeloid leukaemia (AML) is a cancer of the white blood cells (cells that fight against infections). In patients with AML, the bone marrow (the spongy tissue inside the large bones) produces large numbers of abnormal, immature white blood cells called 'blasts'. These abnormal cells quickly build up in large numbers in the bone marrow and are found in the blood.

AML is a life-threatening disease because these immature cells take the place of the normal white blood cells, reducing the patient's ability to fight infections.

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

At the time of designation, AML affected less than 2 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 101,000 people, and is below the threshold 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).

What treatments are available?

Treatment for AML is complex and depends on a number of factors including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. At the time of designation, the main treatment for AML was chemotherapy (medicines to treat cancer). Patients in whom chemotherapy did not work could have a haematopoietic (blood) stem-cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to

[*]Disclaimer: 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 (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 506,500,000 (Eurostat 2010).

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help restore the bone marrow). However, a risk of this procedure is graft-versus-host disease, a potentially fatal complication in which the transplanted cells recognise the patient's cells as 'foreign' and attack them.

The sponsor has provided sufficient information to show that allogeneic T cells encoding an exogenous TK gene might be of significant benefit for patients with AML because it works in a different way to existing treatments and may improve the treatment of patients undergoing haematopoietic stem-cell transplantation. 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?

During haematopoietic stem-cell transplantation used for the treatment of AML, the T cells contained in the graft may be responsible for the graft-versus-host disease.

Allogeneic T cells encoding an exogenous TK gene is an advanced therapy medicine that belongs to the group called 'somatic cell therapy products'. These are medicines that contain cells or tissues that have been manipulated to change their biological characteristics so that they can be used to cure, diagnose or prevent a disease.

This medicine is made of T cells that are extracted from a donor. Before being injected into the patient, a specific T cell sub-population is selected and further manipulated by inclusion of a gene called 'TK suicide gene'. If graft-versus-host disease occurs following transplantation, the TK suicide gene can be activated and will enable the elimination of the T cells that are involved in graft-versus-host disease. The manipulated T cells are then injected into a patient with AML, together with a haematopoietic stem-cell transplant. This is expected to enhance the ability of the stem-cell transplant to replace the cancer cells, while reducing the risk of graft-versus-host disease.

What is the stage of development of this medicine?

The effects of allogeneic T cells encoding an exogenous TK gene have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with allogeneic T cells encoding an exogenous TK gene including patients with AML were ongoing.

At the time of submission, allogeneic T cells encoding an exogenous TK gene was not authorised anywhere in the EU for AML or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 2 June 2010 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

Sponsor's contact details:

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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.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Allogeneic T cells encoding an exogenous TK gene	Treatment of acute myeloid leukaemia
Bulgarian	Алогенни Т-клетки, кодиращи екзогенен ТК ген	Лечение на остра миелоидна левкемия
Czech	Allogenní T lymfocyty kódující exogenní TK gen	Léčba akutní myeloidní leukémie
Danish	Allogene T celler indeholdende et eksogent TK gen	Behandling af akut myeloid leukæmi
Dutch	Allogene T- cellen welke een exogeen TK gen encoderen	Behandeling van acute myeloïde leukemie
Estonian	Allogeensed T-rakud, mis kodeerivad eksogeenset TK geeni	Akuutse müeloidse leukeemia ravi
Finnish	Allogeenisia T-soluja, jotka koodaavat eksogeenista TK-geeniä	Akuutin myelooisen leukemian hoito
French	Cellules T allogéniques codant pour un gène TK exogène	Traitement de la leucémie aiguë myéloïde
German	Allogene T-Zellen, die ein exogenes TK Gen encodieren	Behandlung der akuten myeloischen Leukämie
Greek	Αλλογονικά κύτταρα Τ που φέρουν εξωγενές γονίδιο ΤΚ	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	Exogén TK-gént kódoló allogén T-sejtek	Akut myeloid leukaemia kezelése
Italian	Cellule T allogeniche codificanti un gene timidina-chinasi esogeno	Trattamento della leucemia mieloide acuta
Latvian	Alogēnas, eksogēnu timidīna kināzes (TK) gēnu saturošas T šūnas	Akūtas mieloleikozes ārstēšana
Lithuanian	Alogeninės T ląstelės, koduojančios egzogeninį TK geną	Ūmios mieloleukozės gydymas
Maltese	Ċelluli T alloġeniċi li jikkodifikaw ġene TK esoġenu	Kura tal-lewkimja mjelojda akuta
Polish	Alogeniczne komórki T zawierające egzogenny gen kodujący kinazę tymidynową	Leczenie ostrej białaczki szpikowej
Portuguese	Linfócitos T alogénicos com um gene TK exógeno	Tratamento da leucémia mielóide aguda
Romanian	Celule T alogenice ce codifică o genă TK exogenă	Tratamentul leucemiei mieloide acute
Slovak	Alogénne bunky T kódujúce exogénny gén pre TK	Liečba akútnej myeloickej leukémie
Slovenian	Alogenske T celice s kodo za eksogeni TK gen	Zdravljenje akutne mieloične levkemije
Spanish	Linfocitos T alogénicos que contienen un gen exógneo que codifica TK	Tratamiento de la leucemia mieloide aguda

[1] At the time of designation

Swedish	Allogena T-celler som kodar för den eksogena TK genen	Behandling av akut myeloisk leukemi
Norwegian	Allogene T-celler som koder for eksogent TK gen	Behandling av akutt myelogen leukemi
Icelandic	Ósamgena T frumur sem tjá utanaðkomandi TK gen	Meðferð við bráðu kyrningahvítblæði