European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes for the adjunctive treatment of haematopoietic cell transplantation

On 20 October 2003, orphan designation (EU/3/03/168) was granted by the European Commission to MolMed SpA, Italy, for herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes for the adjunctive treatment of haematopoietic cell transplantation.

What is haematopoietic cell transplantation?

Haematopoietic cells are cells that can produce mature blood cells. They can be found in the bone marrow, the spongy tissue inside the large bones in the body and in low concentrations in the peripheral blood. In certain haematological diseases, where the bone marrow is not able to produce mature blood cells, it is appropriate to use a treatment called transplantation, which consists in replacing the abnormal cells of the immune system and bone marrow with healthy cells generally either from the same person (autologous) or from a donor (allogenic). A severe complication of allogenic haematopoietic cell transplantation is the development of a disease called Graft versus Host Disease (GvHD). This complication involves a reaction between the donor cells (graft) and the recipient's native tissues (host) leading to injury of the recipient's tissues. Severe graft versus host disease can be largely avoided by the removal of certain white blood cells, the so-called T lymphocytes, from the graft before it is administered to the recipient patient. However, a strong reduction of these T cell increases the incidence of disease relapse, rejection of the transplant and occurrence of viral infections. Therefore, in case of relapse, delayed administration of donor T cells may be used. However, severe graft versus host disease represents a relatively frequent and potentially life-threatening complication of delayed infusion of donor T cells.

What are the methods of treatment available?

There are several classes of authorised medicinal products such as anti-infectives (given in order to prevent infection with some viruses or fungi), growth factors, serum-prophylaxis agents, and vaccines, which are used as additional treatment. Gancyclovir is authorised in the Community as an additional treatment (or adjunctive treatment) of the condition, in order to prevent infections with some viruses. However, there are no products authorised to improve the treatment with donor lymphocytes, which may be the case for the product subject to this designation.

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

According to the information provided by the sponsor approximately 8,000 patients are treated with haematopoietic cell transplantation each year in the European Union.

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How is this medicinal product expected to act?
Cells involved in the immune response called T-lymphocytes are isolated from the donor and inoculated (transfected) with a viral gene (herpes simplex 1 virus –thymidine kinase) which makes them particularly susceptible to an antiviral medicine called gancyclovir. Therefore, once these T-lymphocyte cells containing the viral gene are administered to the recipient patient they can be eliminated (destroyed) by treatment with gancyclovir in case that they start to react against the recipient tissues, namely when the risk of the development of graft versus host disease is imminent. Associated to the viral gene, herpes simplex 1 virus-thymidine kinase, these cells receive also an additional gene which is used as a marker for selecting only the cells in which the transfection was successful before the administration to the recipient patient.

What is the stage of development of this medicinal product?
At the time of submission of the application for orphan designation, clinical trials in patients treated with haematopoietic cell transplantation were ongoing.

The proposed medicinal product was not marketed anywhere worldwide for the adjunctive treatment of haematopoietic cell transplantation or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 September 2003 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes	Adjunctive treatment in hematopoietic cell transplantation
Danish	Herpes simplex 1 virus thymidin kinaseog lav affinitet nerve vækstfactor transficeret donor lymfocytter	Adjuvant behandling ved hæmatopoietisk celle transplantation
Dutch	Herpes simplex 1 virus thymidine kinase en getrunceerde zenuw groeifactor receptor met lage affiniteit	Adjunctieve behandeling bij haematopoietische cel transplantatie
Finnish	Herpes simplex 1 virus – tymidiini kinaasi ja typistetyllä, affiniteetiltään alhaislla hermokudoksen kasvutekijäreseptorilla trasfektoidut luovuttajan lymfosyytit	Lisähoito hematopoieettisten solujen transplantaatiossa
French	Lymphocytes du donneur transfectés du gène de la thymidine kinase d'Herpès simplex virus 1 et du gène tronqué du récepteur à basse affinité du facteur de croissance du tissu nerveux	Traitement adjuvant à la transplantation de cellules hématopoïétiques
German	Donorlymphozyten transfiziert mit Thymidinkinase-Gen des Herpes-simplex-Virus vom Serotyp 1 und Genfragment für den niedrigaffinen Rezeptor des Nervenwachstumsfaktors	Ergänzende Behandlung bei hämatopoetischer Stammzelltransplantation
Greek	Γονίδιο της κινάσης της θυμιδίνης του ιού Herpes simplex 1 και ακρωτηριασμένο γονίδιο του υποδοχέα χαμηλής συγγένειας του παράγοντα ανάπτυξης του νεθρικού ιστού, επιμολυσμένων λεμφοκυττάρων δότη	Υποβοηθητική αγωγή κατά την μεταμόσχευση αιματοποιητικών κυττάρων
Italian	Linfociti del donatore transfettati con il gene della timidina kinasi di Herpes simplex virus 1 e il gene troncato del recettore a bassa affinità del fattore di crescita del tessuto nervoso	Trattamento aggiuntivo al trapianto di cellule ematopoietiche
Portuguese	Linfócitos de doador transfectados com o gene da timidina quinase do virús Herpes simplex 1 e gene truncado do receptor de baixa afinidade do factor de crescimento do tecido nervoso	Tratamento adjuvante do transplante de células hematopoiéticas
Spanish	Linfocitos de donante transfectados con el gen de la timidina quinasa del virus Herpes simplex 1 y el gen truncado del receptor de baja afinidad del factor de crecimiento del tejido nervioso	Tratamiento adyuvante del trasplante de células hematopoyéticas
Swedish	Herpes simplex 1 virus tymadinkinas och stympade låg-affinitets nervtillväxtfaktor receptor transfekterade donor lymfocyter	Tilläggsbehandling vid aploidentisk transplantation av hematopoesiska celler