



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 human monoclonal antibody against CD4 for the treatment of cutaneous T cell lymphoma

On 14 April 2004, orphan designation (EU/3/04/198) was granted by the European Commission to Genmab A/S, Denmark, for human monoclonal antibody against CD4 for the treatment of cutaneous T cell lymphoma.

The sponsorship was transferred to Serono Europe Limited, United Kingdom, in April 2006 and subsequently to Genmab A/S, Denmark, in March 2008.

What is cutaneous T cell lymphoma?

Cutaneous T cell lymphoma is a type of cancer of the lymphatic system. The lymphatic system is part of the body's immune system and helps fighting infections. It is a complex system made up of organs such as the bone marrow, the thymus (a gland behind the breast bone), the spleen (an organ in the abdomen, near the stomach), and the lymph nodes (or lymph glands, located throughout the body), which are connected by a network of tiny lymphatic vessels. There are two main types of cells, which make up the lymphatic tissue. These cells are called lymphocytes and belong to the group of white blood cells. The two types are called B lymphocytes (B cells) and T lymphocytes (T cells). Most lymphocytes start growing in the bone marrow. The T cells go from the bone marrow to the thymus where they continue to mature. Cutaneous T-cell lymphoma is a cancer of the T-lymphocytes which mainly affects the skin and most often occurs in people aged between 40 and 60. It is caused by the uncontrolled growth of the T-cells. Cutaneous T-cell lymphoma is a serious and life-threatening condition.

What are the methods of treatment available?

Current treatment for cutaneous T-cell lymphoma can be divided into local treatment and systemic treatment. Local treatments include medicines applied to the skin, therapies using light of a particular wavelength (ultraviolet light) and x-rays. Systemic treatments include medicines such as glucocorticosteroids (a group of medicines that are similar to cortisone), cytotoxic agents (medicines that kill cells), interferon-alfa (a compound that can help the immune system to fight against the cancer cells) and photopheresis (white blood cells are modified by exposure to ultraviolet light). Several products were authorised for the treatment of cutaneous T-cell lymphoma within the Community at the time of submission of the application for orphan drug designation.

Human monoclonal antibody against CD4 might be of potential significant benefit for the treatment of cutaneous T-cell lymphoma because it may act in a different way than other available medicines. This assumption remains to be proven. This will be necessary to maintain the orphan status.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, cutaneous T-cell lymphoma was considered to affect approximately 1 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 39,000 persons.

How is this medicinal product expected to act?

Antibodies are proteins in the body that target specific shapes (receptors) on the surface of foreign bodies, such as bacteria or cancer cells. Human monoclonal antibody against CD4 is a human protein (immunoglobulin) that is able to recognise and bind to a receptor present on the surface of T cells; the receptor is called CD4. The union of the receptor and the antibody would trigger a reaction that would end in the destruction of the cells that bear this receptor. In the case of cutaneous T cell lymphoma, these CD4 receptor-containing cells are those that show an uncontrolled growth (proliferation). Although the mechanisms through which the cells are killed have not been fully explained it seems that the union of the antibody and the receptor could have two effects, first the stimulation of other specific T cells (the so-called natural killer cells) aimed to destroy abnormal cells and secondly the inhibition of the proliferation of T cells that bear the CD4 receptor.

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 with cutaneous T cell lymphoma were ongoing.

Human monoclonal antibody against CD4 was not marketed anywhere worldwide for cutaneous T cell lymphoma 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 16 March 2004 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.

For more information:

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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.

Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Human monoclonal antibody against CD4	Treatment of cutaneous T-cell lymphoma
Danish	Humant monoklonalt antistof mod CD4	Behandling af kutant T-celle-lymfom
Dutch	Humane monoklonale antilichamen tegen CD4	Behandeling van cutaan T-cel-lymfoom
Finnish	Ihmisperäinen monoklonaalinen vasta-aine CD4:lle	Ihon T-solulymfooman hoito
French	Anticorps monoclonal humain dirigé contre les CD4	Traitement des lymphomes cutanés à cellules T
German	Humaner monoklonaler Anti-CD4-Antikörper	Behandlung von kutanem T-Zell-Lymphom
Greek	Μονοκλωνικό αντίσωμα κατά του CD4	Θεραπεία του δερματικού λεμφώματος T κυττάρων
Italian	Anticorpo monoclonale umano anti-CD4	Trattamento del linfoma cutaneo a cellule T
Portuguese	Anticorpo monoclonal humano anti-CD4	Tratamento do linfoma cutâneo das células T
Spanish	Anticuerpo monoclonal humano anti-CD4	Tratamiento de linfoma cutáneo de células T
Swedish	Human monoclonal CD4-antikropp	Behandling av kutant T-cellslymfom