



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin for the treatment of follicular lymphoma

On 28 August 2006, orphan designation (EU/3/06/394) was granted by the European Commission to Analytica International GmbH, Germany, for autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin for the treatment of follicular lymphoma.

The sponsorship was transferred to Analytica International Inc. - Outcomes Research and Pricing, Germany, in May 2011 and subsequently to Biovest Europe Limited, United Kingdom, in September 2011.

What is follicular lymphoma?

Follicular 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). There are several different types of lymphomas. In follicular lymphoma, the cancer cells are related to the B-lymphocytes. Follicular lymphoma is a life-threatening disease.

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

At the time of designation follicular lymphoma affected approximately 2.2 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 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 knowledge of the Committee for Orphan Medicinal Products (COMP).

* 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 459,700,000 (Eurostat 2004).



What treatments are available?

At the time of submission of the application for orphan drug designation, several medicinal products were authorised in the European Union for use in follicular lymphoma. The choice of treatment depends in particular on the extension of the disease as well as on the responses to therapies previously prescribed.

Autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin might be of potential significant benefit for the treatment of follicular lymphoma because it may act in a different way from other available medicines and it might improve the long-term outcome of the patients. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

The medicinal product is a vaccine that contains proteins originating from the cancer cells of the patient him/herself and the copper-containing respiratory protein, keyhole limpet haemocyanin, from the gastropod (mollusc) *Megathura crenulata*. According to the sponsor, a specific protein from the surface of the cancer cells is isolated and manipulated in the laboratory to be further injected back into the patient. It is expected that following the injection of this "patient-specific vaccine", the body's defence system (immune system) will recognise this cancer cell protein as a foreign body and will react against it by producing specific antibodies. It is expected that after vaccination, the immune system will not only recognise the vaccine as foreign, but also the cancer cells that carry the same surface protein as that used to prepare the patient-specific vaccine. The patient body's immune system could then kill these cancer cells.

What is the stage of development of this medicine?

The evaluation of the effects of autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin in experimental models is ongoing.

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

Autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin was not authorised anywhere worldwide for treatment of follicular lymphoma or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 July 2006 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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin	Treatment of follicular lymphoma
Bulgarian	Автоложен имуноглобулинов идиотип с туморен произход, свързан към хемоцианин от <i>Megathura crenulata</i>	Лечение на фоликулярен лимфом
Czech	Autologní z tumoru odvozený imunoglobulin idiotypu KLH (keyhole limpet hemocyanin)	Léčba folikulárního lymfomu
Danish	Autologt tumorderiveret immunoglobulin idiotype koblet til "keyhole limpet haemocyanin"	Behandling af follikulært lymfom
Dutch	Autologe tumor afgeleid immunoglobuline idiotype gekoppeld aan "keyhole limpet haemocyanin"	Behandeling van folliculair lymfoom
Estonian	Autoloogne kasvajaist pärinev immunoglobuliini idiotüüp seotud "keyhole limpet haemocyanin"-iga	Follikulaarse lümfoomi ravi
Finnish	Autologinen, kasvaimesta tehty, KLH (keyhole limpet hemocyanin) -kytketty immunoglobuliinin idiotyyppi	Follikulaarisen lymfooman hoito
French	Idiotype de l'immunoglobuline autologue d'origine tumorale conjugué à l'hémocyanine de <i>Megathura crenulata</i>	Traitement des lymphomes folliculaires
German	Autologer tumoraler Immunglobulin-Idiotyp KLH gekoppelt an <i>Megathura crenulata</i> (keyhole limpet) Haemocyanin	Behandlung von follikulärem Lymphom
Greek	Προερχόμενος από όγκο, αυτόλογος γονότυπος ανοσοσφαιρίνης συνδεδεμένος με την αιμοκυανίνη «keyhole limpet»	θεραπεία του θηλακιδώδους λεμφώματος
Hungarian	KLH-val (keyhole limpet haemocyanin) kapcsolt autológ tumor eredetű idiotípusú immunglobulin	Follicularis lymphoma kezelése
Italian	Idiotipo di immunoglobulina derivato da tumore autologo, accoppiato all'emocianina di <i>Megathura crenulata</i> (keyhole limpet)	Trattamento del linfoma follicolare
Latvian	Autogēnais audzējšūnu imunoglobulīns, kas savienots ar <i>Megathura crenulata</i> hemocianīnu (KLH)	Folikulārās limfomas ārstēšana
Lithuanian	Su KLH konjuguotas imunoglobulinas, prieš autologinį iš tumoro išskirtą idiotipą	Folikulinės limfomos gydymas

¹ At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Maltese	Idjotip ta' immunoglobulina derivata minn tumor awtologu magħqud mal-emoċjanina ta' <i>Megathura crenulata</i> (keyhole limpet)	Kura tal-linfoma follikulari
Polish	Autologiczna immunoglobulina z chłoniaka, o charakterze idiotypowym KLH (keyhole limpet hemocyanin)	Leczenie chłoniaków grudek
Portuguese	idiotipo de imunoglobulina derivada de tumor autólogo combinado com hemocianina de <i>Megathura crenulata</i>	Tratamento do linfoma folicular
Romanian	Idiotip de imunoglobulină de origine tumorală autologă, conjugat cu hemocianina extrasă din <i>Megathura crenulata</i>	Tratamentul limfomului folicular
Slovak	Autológny z tumoru odvodený idiotypický imunoglobulín v kombinácii s KLH (keyhole limpet haemocyanin)	Liečba folikulárneho lymfómu
Slovenian	Avtologni, iz tumorskih celic pridobljeni idiotip imunoglobulina, vezan na KLH (keyhole limpet haemocyanin)	Zdravljenje folikularnega limfoma
Spanish	Idiotipo de inmunoglobulina derivado de tumor autólogo combinado con hemocianina <i>Megathura crenulata</i>	Tratamiento del linfoma folicular
Swedish	Autolog tumörhärledd idiotyp immunoglobulin kopplat till <i>Megathura crenulata</i> hemocyanin	Behandling av follikulärt lymfom
Norwegian	Autolog tumorderivert idiotype immunoglobulin koblet til <i>Megathura crenulata</i> hemocyanin	Behandling av follikulært lymfom
Icelandic	Eigið æxlis-afleitt immúnóglóbúlín idiótýpískt KLH	Meðferð á follicular eitilfrumukrabbameini