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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet hemocyanin for the treatment of mantle cell lymphoma

On 23 February 2011, orphan designation (EU/3/10/831) was granted by the European Commission to Analytica International Inc, Germany, for autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet hemocyanin for the treatment of mantle cell lymphoma.

The sponsorship was transferred to Biovest Europe Limited, United Kingdom, in September 2011.

What is mantle cell lymphoma?

Mantle cell lymphoma is an aggressive cancer of a type of white blood cell called B-lymphocytes, or B cells. In mantle cell lymphoma, the B cells multiply too quickly and live for too long, so there are too many of them in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin area, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats.

Mantle cell lymphoma is usually diagnosed in people aged over 50 years. It is more common in men than women. Mantle cell lymphoma is a severe and life-threatening disease that is associated with poor overall survival.

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

At the time of designation, mantle cell lymphoma affected less than 0.3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 15,000 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).

What treatments are available?

At the time of designation, temsirolimus was specifically authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or has not responded to other

*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).

treatments. The main treatments for mantle cell lymphoma included chemotherapy (medicines to treat cancer), immunotherapy (medicines that stimulate the body's own immune system to kill the cancer cells) and radiotherapy (treatment with radiation). Haematopoietic (blood) stem cell transplantation was also used. This is a complex procedure where patients receive stem cells to help restore the bone marrow.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit to those affected by the condition because early studies show that it works in a different way to existing treatments, by inducing an immune response which may fight against the cancerous B cells. 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 medicine is a 'cancer vaccine'. It is expected to work by activating the patient's immune system (the body's natural defences) so that it attacks and kills the cancer cells.

To prepare this medicine, cancer cells are extracted from a patient's lymph node. A protein specific to the patient's cancer cells is isolated from the cells, then attached to a carrier, 'keyhole limpet haemocyanin' (a protein prepared from a sea snail), to enhance the response of the body to the vaccine.

When this 'patient-specific' vaccine is given, the patient's immune system is expected to recognise the cancer cell protein as 'foreign'. This is expected to stimulate an immune response against the cancer cells, resulting in the immune system attacking them in the body.

What is the stage of development of this medicine?

The effects of autologous tumor-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, one clinical trial in patients with mantle cell lymphoma had been carried out.

At the time of submission, this medicine was not authorised anywhere in the EU for the treatment of mantle cell lymphoma. Orphan designation of this medicine had been granted for the treatment of mantle cell lymphoma in the United States of America (USA), and for the treatment of follicular lymphoma in the EU and the USA.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet hemocyanin	Treatment of mantle cell lymphoma
Bulgarian	Автоложен имуноглобулинов идиотип с туморен произход, свързан към хемоцианин от <i>Megathura crenulata</i>	Лечение на мантелно-клетъчна лимфома
Czech	Autologní z tumoru odvozený imunoglobulin idiotypu KLH (keyhole limpet hemocyanin)	Léčba lymfomu z plášťové zóny
Danish	Autologt tumorderiveret immunoglobulin idiotype koblet til "keyhole limpet haemocyanin"	Behandling af mantelcellelymfom
Dutch	Autologe tumor afgeleid immunoglobuline idiotype gekoppeld aan "keyhole limpet haemocyanin"	Behandeling van mantelcellymfoom
Estonian	Autoloogne kasvaja pärinev immunoglobuliini idiotüüp seotud "keyhole limpet haemocyanin"-iga	Mantelrakulise lümfoomi ravi
Finnish	Autologinen, kasvaimesta tehty, KLH (keyhole limpet hemocyanin) -kytketty immunoglobuliinin idiotyyppi	Manttelisolu-lymfooman hoito
French	Idiotype de l'immunoglobuline autologue d'origine tumorale conjugué à l'hémocyanine de <i>Megathura crenulata</i>	Traitement des lymphomes du manteau
German	Autologer tumoraler Immunglobulin-Idiotyp KLH gekoppelt an <i>Megathura crenulata</i> (keyhole limpet) Haemocyanin	Behandlung von Mantelzelllymphom
Greek	Προερχόμενος από όγκο, αυτόλογος γονότυπος ανοσοσφαιρίνης συνδεδεμένος με την αιμοκυανίνη «keyhole limpet»	Θεραπεία του λεμφώματος μανδουκών κυττάρων
Hungarian	KLH-val (keyhole limpet hemocyanin) kapcsolt autológ tumor eredetű idiotípusú immunoglobulin	Köpenyseztes lymphoma kezelése
Italian	Idiotipo di immunoglobulina derivato da tumore autologo, accoppiato all'emo-cianina di <i>Megathura crenulata</i> (keyhole limpet)	Trattamento del linfoma con cellule a mantello
Latvian	Autogēnais audzējšūnu imunoglobulīns, kas savienots ar <i>Megathura crenulata</i> hemocianīnu (KLH)	Mantijšūnu limfomas ārstēšana
Lithuanian	Su KLH konjuguotas imunoglobulinas, prieš autologinį iš tumoro išskirtą idiotipą	Mantijos ląstelių limfomos gydymas
Maltese	Idjotip ta' immunoglobulina derivata minn tumur awtologu magħqud mal-emoċjanina ta' <i>Megathura crenulata</i> (keyhole limpet)	Kura tal-linfoma taċ-ċelloli tal-mantell
Polish	Autologiczna immunoglobulina z chłoniaka, o charakterze idiotypowym KLH (keyhole limpet hemocyanin)	Leczenie chłoniaków z komórek płaszczowych
Portuguese	idiotípo de imunoglobulina derivada de tumor autólogo combinado com hemocianina de <i>Megathura</i>	Tratamento de linfoma de células do manto

¹ At the time of designation

Language	Active ingredient	Indication
	<i>crenulata</i> .	
Romanian	Idiotip de imunoglobulină de origine tumorală autologă, conjugat cu hemocianina extrasă din <i>Megathura crenulata</i>	Tratamentul limfomului cu celule în manta
Slovak	Autológny z tumoru odvodený idiotypický imunoglobulín v kombinácii s KLH (keyhole limpet haemocyanin)	Liečba lymfómu plášťovej zóny
Slovenian	Avtologni, iz tumorskih celic pridobljeni idiotip imunoglobulina, vezan na KLH (keyhole limpet haemocyanin)	Zdravljenje limfoma plaščnih celic
Spanish	Idiotipo de inmunoglobulina derivado de tumor autólogo combinado con hemocianina <i>Megathura crenulata</i>	Tratamiento del linfoma de células del manto
Swedish	Autolog tumörhärledd idiotyp immunoglobulin kopplat till <i>Megathura crenulata</i> hemocyanin	Behandling av mantelcellslymfom
Norwegian	Autolog tumorderivert idiotype immunoglobulin koblet til <i>Megathura crenulata</i> hemocyanin	Behandling av mantelcelle-lymfom
Icelandic	Eigið æxlis-afleitt immúnóglóbúlín idiótýpískt KLH	Meðferð möttulfrumu eitlakraðbameins