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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)

On 9 August 2012, orphan designation (EU/3/12/1038) was granted by the European Commission to AOP Orphan Pharmaceuticals AG, Austria, for recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated).

What is peripheral T-cell lymphoma?

Peripheral T-cell lymphoma is a cancer of the lymphatic system, a network of vessels that transport fluid from tissues through the lymph nodes and into the bloodstream. In peripheral T-cell lymphoma there is uncontrolled growth of T lymphocytes (T cells), a type of white blood cell found in the lymphatic system, which appear in the blood circulating in peripheral parts of the body. Different types of peripheral T-cell lymphoma have been identified and categorised as nodal, other extranodal and leukaemic/disseminated.

The symptoms of the disease vary according to the type of lymphoma, but the first sign is usually a lump in the neck, under the arm or in the groin area, which is caused by an enlarged lymph node. The lymphoma may also affect other organs in the body such as the bone marrow, liver and the skin.

Peripheral T-cell lymphoma is a serious and life-threatening condition because in most cases the disease comes back within one year after initial treatment and is associated with poor overall survival.

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

At the time of designation, peripheral T-cell lymphoma affected less than 1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 51,000 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).

[*]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 506,300,000 (Eurostat 2011).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

At the time of designation, there were no specific treatments for peripheral T-cell lymphoma, but the disease was treated in the same way as the broader class of lymphomas known as non-Hodgkin's lymphomas, for which several medicines were authorised in the EU. The main treatment was chemotherapy (medicines to treat cancer), sometimes in combination with radiotherapy (treatment with radiation).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with peripheral T-cell lymphoma because it works in a different way to existing treatments and early studies in experimental models suggest it may have anti-tumour activity that is specifically targeted to T 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?

This medicine contains a toxin (a substance toxic for cells) called diphtheria toxin, which has been 'fused' to fragments of a monoclonal antibody, a type of protein that has been designed to recognise and attach to a specific structure. The monoclonal antibody fragments in this medicine are expected to attach to a protein called CD3, which is found on the surface of certain T cells. The monoclonal antibody fragments carry the toxin to the CD3-positive T cells, which are found on most peripheral T-cell lymphomas. Once taken up by the T cells, the toxin is expected to kill the cancer cells.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with peripheral T-cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for peripheral T-cell lymphoma 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 11 July 2012 recommending the granting of this designation.

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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:

AOP Orphan Pharmaceuticals AG
Wilhelminenstrasse 91/IIf
A-1160 Vienna
Austria
Telephone: +43 1 503 72 44 10
Telefax: +43 1 503 72 44 61
E-mail: office@aoporphan.at

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	Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein	Treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)
Bulgarian	Рекомбинантен анти-CD3 дву-единична –верига- FV-дифтериен токсин фюжън протеин	Лечение на периферен Т-клетъчен лимфом (левкемизирал, нодален, екстранодален)
Czech	Rekombinantní scFv bispecifická protilátka proti CD3 ve fúzi s difterickým toxinem	Léčba periferních T- lymfomů (leukemický, nodální, extranodální)
Danish	Rekombinant anti-CD3-bi-enkel-kæde- Fv-difteri toksin fusionsprotein	Behandling af perifert T-celle lymfom (nodal, extranodal og leukæmisk /dissemineret))
Dutch	Recombinant anti-CD3-bi-enkelstrengig -Fv-diphtherie-toxine fusie-proteïne	Behandeling van perifere T-cel lymfoma (nodale, andere extranodale en leukemisch/gedissemineerd)
Estonian	Rekombinantne anti-CD3-bi-üksikahelaline-Fv-difteeriatoksiini fusioonproteiin	Perifeerse T-rakulise lümfoomi (, nodulaarne, ekstranodulaarsed ja leukeemilised/dissemineeruvad) ravi
Finnish	Rekombinantti anti-CD3-bi-yksiketjuinen Fv-difteriatoksiinifuusioproteiini	Perifeerisen T-solulymfooman hoito (leukeeminen, nodaalinen, ekstranodaalinen)
French	Protéine recombinante issue de la fusion de toxine de diphtérie et FV à chaine simple anti-CD3	Traitement du lymphome périphérique à cellules T (, nodulaire, extra nodulaire, et leucémique/disséminé)
German	Rekombinantes Anti-CD3 (bi-spezifisches single-chain-variable fragment (scFv))-Diphterietoxin Fusionsprotein	Behandlung des Peripheren T-Zell-Lymphoms (nodal, extranodal und leukämisch/disseminiert)
Greek	Ανασυνδυασμένοτμήμα αντισώματος anti-CD3 δύο μονών αλυσίδων Fv συζευγμένων με την τοξίνη της εδιφθερίτιδας	Θεραπεία του λεμφώματος περιφερικών κυττάρων Τ (λεμφαδενικό, άλλο εκτός λεμφαδένων και λευχαιμικό/ διάσπαρτο)
Hungarian	Rekombináns, anti-CD3, egyláncú, Fv diftéria toxin	Perifériás T-sejtes lymphoma (nodális, egyéb extranodális és leukaemiás/disszeminált)

[1] At the time of designation

Language	Active ingredient	Indication
	fúziós fehérje	kezelése
Italian	Proteina di fusione contenente una tossina difterica e un frammento dimerico variabile a singola catena ricombinante anti-CD3	Trattamento del linfoma periferico a cellule T (leucemico, nodale, extranodale)
Latvian	Rekombinēts anti-CD3 div-/vienķēdes Fv-diftērijas toksīna saplūšanas proteīns	Perifēriskās T-šūnu limfomas (leikēmiskas, nodulāras, ekstranodulāras) ārstēšana
Lithuanian	Rekombinantinis prieš-CD3 bi-viengrandinis Fv difterijos toksino sintezės baltymas	Periferinės T-ląstelių limfomos (mazginės, kitų ne mazginės ir leukeminės/diseminuotos), gydymas
Maltese	Proteina tal-fużjoni rikombinanti magħmula minn tossina difterika u framment dimeriku varjabbli b'katina wahda kontra CD3	Kura tal-limfoma periferali taċ-ċelloli tat-tip T (fin-nodi, oħrajn barra n-nodi u lewkemiċi/mxerrda)
Polish	Rekombinowane białko fuzyjne toksyny błonicy oraz dwóch jednołańcuchowych anty-CD3-Fv	Leczenie obwodowego chłoniaka T-komórkowego (białaczkopodobny, węzłowy, pozawęzłowy)
Portuguese	Proteína de fusão recombinante da toxina diftérica de FV de cadeia única anti-CD3 biespecífico	Tratamento do linfoma periférico das células T (leucémico, nodular, extra nodular)
Romanian	Proteina recombinantă de fuziune a toxinei difterice cu două Fv de anti-CD3 cu catenă simplă	Tratamentul limfomului periferic cu celule T (ganglionar, extraganglionar şi leucemic/diseminat)
Slovak	Rekombinantná scFv bišpecifická protilátka proti CD3 vo fúzii s difterickým toxínom	Liečba periférneho T-bunkového lymfómu (leukemického, nodálneho, extranodálneho)
Slovenian	Rekombinantni fuzijski protein, sestavljen iz dveh enoverižnih anti-CD3-Fv in toksina davice	Zdravljenje perifernega limfoma celic T (levkemični, nodalni, ekstranodalni)
Spanish	Proteína de fusión recombinante compuesta por dos cadenas simples de Fv anti CD3 y toxina diftérica	Tratamiento del linfoma periférico de células T (ganglionar, extraganglionare , leucémico-diseminado)
Swedish	Rekombinant anti-CD3-bi-enkelkedje-Fv-difteritoxin fusionsprotein	Behandling av perifert T-cellslymfom (nodalt, annat extranodalt och leukemiskt/disseminerat))
Norwegian	Rekombinant anti-CD3-bi-enkel-kjede- Fv-difteri toksin	Behandling av perifert T-cellelymfom (nodalt, annet ekstranodalt og leukemisk/disseminert)

Language	Active ingredient	Indication
	fusionsprotein	
Icelandic	Raðbrigða anti-CD3- bí -einkeðju -Fv-barnaveikis eiturefnis samrunaprótein	Meðferð á útlægu T-frumu eitlakrabbameini (í eitlum, utan eitla og hvítblæði/dreift)