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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 cutaneous T-cell lymphoma

On 9 August 2012, orphan designation (EU/3/12/1039) 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 cutaneous T-cell lymphoma.

What is cutaneous T-cell lymphoma?

Cutaneous T-cell lymphoma (CTCL) 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 CTCL there is uncontrolled growth of the T lymphocytes (T cells), a type of white blood cell found in the lymphatic system. The cancerous T cells appear in the skin, causing lesions (rashes, plaques and tumours) which can be itchy and painful.

CTCL usually happens in people aged between 40 and 60 years. In many cases, the disease is long lasting, however, it can be a serious and life-threatening disease because it can develop into more aggressive forms of cancer and may have a large impact on quality of life, particularly because the skin lesions can cause disfigurement.

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

At the time of designation, CTCL 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).

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What treatments are available?

At the time of designation, several products were authorised for the treatment of CTCL within the EU. Treatments for CTCL can be divided into topical (applied to the skin) and systemic (affecting the whole body):

- topical treatments include topical corticosteroids, the topical anticancer medicine carmustine, ultraviolet light and X-rays;
- systemic treatments include cytotoxic medicines (medicines that kill cells that are dividing, such as cancer cells) and interferon alfa (a medicine that helps the immune system to fight against the cancer cells).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with CTCL because it works in a different way to existing treatments and early studies suggest it may improve patients' condition. 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 for the toxin to the CD3-positive T cells, which are found on most CTCLs. 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 CTCL were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for CTCL 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:

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein	Treatment of cutaneous T-cell lymphoma
Bulgarian	рекомбинантен анти-CD3 дву-единична – верига- FV-дифтериен токсин фюжън протеин	Лечение на кожен Т-клетъчен лимфом
Czech	Rekombinantní scFv bispecifická protilátka proti CD3 ve fúzi s difterickým toxinem	Léčba kožního T-lymfomu
Danish	Rekombinant anti-CD3-bi-enkel-kæde- Fv-difteri toksin fusionsprotein	Behandling af kutant T-celle-lymfom
Dutch	Recombinant anti-CD3-bi-enkelstrengig-Fv-diphtherie-toxine fusie-proteïne	Behandeling van cutaan T-cel-lymfoom
Estonian	Rekombinantne anti-CD3-bi-üksikahelaline-Fv-difteeriatoksiini fusioonproteiin	Kutaanse T-rakulise lümfoomi ravi
Finnish	Rekombinantti anti-CD3-bi-yksiketjuinen Fv-difteriatoksiinifuusioproteiini	Ihon T-solulymfooman hoito
French	Protéine recombinante issue de la fusion de toxine de diphtérie et FV à chaine simple anti-CD3	Traitement des lymphomes cutanés à cellules T
German	Rekombinantes Anti-CD3 (bi-spezifisches single-chain-variable fragment (scFv))-Diphterietoxin Fusionsprotein	Behandlung von kutanem T-Zell-Lymphomen
Greek	Ανασυνδυασμένο τμήμα αντισώματος anti-CD3 δύο μονών αλυσίδων Fv συζευγμένων με την τοξίνη της εδιφθερίτιδας	Θεραπεία του δερματικού λεμφώματος Τα κυττάρων
Hungarian	Rekombináns, anti-CD3, bi egyláncú, Fv diftéria toxin fúziós fehérje	T-sejtes kután lymphoma kezelése
Italian	Proteina di fusione ricombinante contenente una tossina difterica e un frammento dimerico variabile a singola catena anti-CD3	Trattamento del linfoma cutaneo a cellule T
Latvian	Rekombinēts anti-CD3 div-/vienķēdes Fv-diftērijas toksīna saplūšanas proteīns	Ādas T-šūnu limfomas ārstēšana
Lithuanian	Rekombinantinis prieš-CD3 bi- viengrandis-Fv-difterijos toksino sintezės baltymas	Odos T ląstelių limfomos gydymas
Maltese	Proteina tal-fużjoni rikombinanti magħmula minn tossina difterika u framment dimeriku varjabbli b'katina wahda kontra CD3	Kura tal-limfoma taċ-ċelluli tat-tip T tal-ġilda
Polish	Rekombinowane białko fuzyjne toksyny błonicy oraz dwóch jednołańcuchowych anty-CD3-Fv	Leczenie chłoniaka skórnego T-komórkowego
Portuguese	Proteína de fusão recombinante da toxina diftérica de FV de duas cadeias únicas anti-CD3	Tratamento do linfoma cutâneo de células T
Romanian	Proteina recombinantă de fuziune a toxinei difterice cu două Fv de anti-CD3 cu catenă simplă	Tratamentul limfomului cutanat cu celule T

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Rekombinantná scFv bišpecifická protilátka proti CD3 vo fúzii s difterickým toxínom	Liečba kutánneho T-bunkového lymfómu
Slovenian	Rekombinantni fuzijski protein, sestavljen iz dveh enoverižnih anti-CD3-Fv in toksina davice	Zdravljenje kožnega T-celičnega limfoma
Spanish	Proteína de fusión recombinante compuesta por dos cadenas simples de Fv anti CD3 y toxina diftérica	Tratamiento del linfoma cutáneo de células T
Swedish	Rekombinant anti-CD3-bi-enkelkedje-Fv-difteritoxin fusionsprotein	Behandling av kutant T-cellslymfom
Norwegian	Rekombinant anti-CD3-bi-enkel-kjede- Fv-difteri toksin fusionsprotein	Behandling av kutan T-celle lymfom
Icelandic	Raðbrigða anti-CD3-bí-einkeðju-Fv-barnaveikis eiturefnis samrunaprótein	Meðhöndlun á T-frumu húð eitlakrabba