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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pralatrexate for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)

On 13 April 2007, orphan designation (EU/3/07/444) was granted by the European Commission to Oxford Regulatory Solutions Ltd, United Kingdom, for pralatrexate for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated).

The sponsorship was transferred to European Medical Advisory Services Limited, United Kingdom, in December 2007 and subsequently to Allos Therapeutics Limited, United Kingdom, in April 2010.

What are peripheral T-cell lymphomas (nodal, other extranodal and leukaemic/disseminated)?

Peripheral T-cell lymphoma belongs to the group of non-Hodgkin's lymphomas, which are cancers originating from the lymphatic system. The lymphatic system is part of the body's immune system and helps to fight 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). The main type of cells in the lymphatic tissue are called lymphocytes, and belong to the broader group of white blood cells. There are two main types of lymphocytes: the B lymphocytes (B cells), and the T lymphocytes (T cells). Normally, the lymphatic cells grow in a controlled manner. Peripheral T-cell lymphoma is caused by the uncontrolled growth of T-lymphocytes, in different stages of maturity. Several different types of peripheral T-cell lymphomas have been identified and categorised (nodal, other extranodal and leukaemic/disseminated). Patients most often present with generalised lymph node enlargement, liver enlargement and bone marrow involvement; sometimes fever is present. Peripheral T-cell lymphoma is a serious and life-threatening condition.

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

At the time of designation, peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated) affected less than 1 in 10,000 people in the European Union (EU)*. This is

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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equivalent to a total of fewer than 46,000 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

There are currently several medicinal products authorised in the Community for treatment of non-Hodgkin lymphoma. The choice of treatment depends in particular on the extension of the disease as well as on the response to therapies previously prescribed. Although chemotherapy (using medicines to kill cancer cells) is the current standard of care for peripheral T-cell lymphoma, most tumours will come back, and then more intensive treatments are given, using several chemotherapeutic agents together.

Pralatrexate might be of potential significant benefit for the treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated) because it acts as other drugs used currently for the treatment of the condition but might have a different activity. This 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?

Enzymes are proteins produced by the cells of the body that speed up the conversion of certain substances into other substances. Pralatrexate inhibits (blocks) the activity of an enzyme, called dihydrofolate reductase, which is necessary for cell growth and multiplication. As these enzymes are less available to help many chemical reactions in growing cells, this might lead to the arrest of cell growth. Since peripheral T-cell lymphoma is caused by the uncontrolled growth of the T-lymphocytes, pralatrexate might help in slowing down or stopping this uncontrolled cell growth.

What is the stage of development of this medicine?

The effects of pralatrexate were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with peripheral T cell lymphoma (nodal, other extranodal and leukaemic/disseminated) were ongoing.

Pralatrexate was not authorised anywhere in the world for the treatment of peripheral T-cell lymphoma, at the time of submission. Orphan designation of pralatrexate was granted in the United States for the treatment of T-cell lymphoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 March 2007 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 European Union) 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	Pralatrexate	Treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)
Bulgarian	Пралатрексат	Лечение на периферен Т-клетъчен лимфом (нодален, екстранодален и левкемизирал/дисеминиран)
Czech	Pralatrexat	Léčba periferních T- lymfomů (nodální, extranodální a leukemické/diseminované)
Danish	Pralatrexat	Behandling af perifer T-celle lymfom (nodal, andre extranodale og leukæmiske/disseminerede)
Dutch	Pralatrexate	Behandeling van perifere T-cel lymfomen (nodale, andere extranodale en leukemische/uitgezaaïde)
Estonian	Pralatreksaat	Perifeerse T-rakulise lümfoomi (nodulaarne, teised ekstranodulaarsed ja leukeemilised/dissemineerunud) ravi
Finnish	Pralatreksaatti	Perifeerisen T-solulymfooman hoito (nodaalinen, muu ekstranodaalinen ja leukeeminen/ disseminoitunut)
French	Pralatrexate	Traitement du lymphome périphérique à cellules T (nodulaire, autre extra nodulaire et leucémique/disséminé)
German	Pralatrexat	Behandlung des peripheren T-Zell-Lymphoms (nodulär, extranodulär und leukämisch/disseminiert)
Greek	Πραλατρεξάτη	Θεραπεία του λεμφώματος περιφερικών κυττάρων Τ (λεμφαδενικό, άλλο εκτός λεμφαδένων και λευχαιμικό/ διάσπαρτο)
Hungarian	Pralatrexat	Perifériás T-sejtes lymphoma (nodalis, egyéb extranodalis és leukémiás/disszeminált) kezelése
Italian	Pralatrexato	Trattamento del linfoma periferico a cellule T (nodale, altre forme extranodali e leucemico/disseminato)
Latvian	Pralatreksāts	Perifēriskās T-šūnu limfomas (nodulāras, citas ekstranodulāras un leikēmiskas / diseminētas) ārstēšana
Lithuanian	Pralatreksatas	Periferinės T-ląstelių limfomos (mazginės, kitos ne mazginės ir leukeminės/difuzinės) gydymas
Maltese	Pralatrexate	Kura tal-limfoma taċ-ċelloli T periferali (fin-nodi, oħrajn barra n-nodi u lewkemiċi/imxerrdin)
Polish	Pralatreksat	Leczenie obwodowego chłoniaka T-komórkowego (węzłowy, inny pozawęzłowy i białaczkopodobny/rozsiany)
Portuguese	Pralatrexato	Tratamento do linfoma periférico das células T (nodulares, outros extra nodulares e leucémicos/disseminados)
Romanian	Pralatrexat	Tratamentul limfomului periferic cu celule T (ganglionar, extraganglionar şi leucemic/diseminat)
Slovak	Pralatrexát	Liečba periférneho T-bunkového lymfómu (nodálneho, iného extranodálneho a leukemického/diseminovaného)

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Slovenian	Pralatreksat	Zdravljenje perifernega limfoma celic T (nodalni, ekstranodalni, levkemični/diseminirani)
Spanish	Pralatrexato	Tratamiento del linfoma periférico de células T (ganglionar, otros extraganglionares, leucémico/diseminado)
Swedish	Pralatrexat	Behandling av perifert T-cellslymfom (nodal, andra extranodala och leukemisk/spridd)
Norwegian	Pralatreksat	Behandling av perifert T-celle-lymfom (nodalt, annet ekstranodalt og leukemisk/disseminert)
Icelandic	Pralatrexat	Meðferð við útlægu T-eitilfrumukrabbameini (í eitlum, utan þeirra og hvítblæðis/dreift)