15 November 2010
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

thalidomide for the treatment of erythema nodosum lepra or type II lepra reactions

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in November 2010 on request of the sponsor.

On 20 November 2001, orphan designation (EU/3/01/066) was granted by the European Commission to Pharmion Ltd., United Kingdom, for thalidomide for the treatment of erythema nodosum lepra or type II lepra reactions.

The sponsorship was transferred to Celgene Europe Limited, United Kingdom, in December 2008.

What is erythema nodosum lepra or Type II lepra reactions?

Leprosy is a chronic infectious disease caused by the bacterium *Mycobacterium leprae*. The infection affects the skin, nerves (e.g. of the limbs) and mucous membranes (membranes that line various body cavities exposed to the external environment and internal organs). Patients develop multiple lesions accompanied by sensory loss in the affected areas that usually begins in the extremities (toes, fingertips). Erythema nodosum lepra (ENL)/ type II lepra reactions stems from a complication of the immune system that occurs in patients with leprosy. The condition may involve many parts of the body but almost always affects the skin. ENL develops rapidly over a few hours when the skin on the arms, forearms, face, trunk and thighs can be covered in painful red papules. In severe attacks the majority of the body is covered in dark papules that intensify in colour over 2-3 days before subsidising, leaving the affected area of skin darkly stained. Episodes are usually associated with fever and general malaise and sometimes other organs, such as the joints, eyes, kidneys, and lymphatics are affected. About 50% of patients with ENL develop painful neuritis (inflammation of the nerves) and increased nerve functional impairment. Painful enlargement of lymph nodes, liver and spleen may occur, as well as episcleritis (inflammation of the outer coating of the eye) and iridocyclitis (inflammation of the iris; the part of the eye with colour). ENL reactions may be of all degrees of severity being almost unnoticed in some, but in others occurring continuously, and if left untreated, may lead to gross weakness and occasionally death. The condition is chronically debilitating.

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

At the time of designation, erythema nodosum lepra or Type II lepra reactions affected approximately 0.02 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 750 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?

Rifampicin, dapsone and clofazimin are authorised for the treatment of erythema nodosum lepra in the Community. In addition, corticosteroids and thalidomide are not authorised but are used. Thalidomide could be of potential significant benefit for the treatment of erythema nodosum lepra. The main reason for this potential is thalidomide's mechanism of action that could provide additional relief of the symptoms. 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?

Although the mechanism of action of thalidomide in leprosy is not fully understood, it is thought to involve tumour necrosis factor-alpha (TNF-alpha). TNF-alpha is a molecule that controls the activation of immune system and patients with erythema nodosum lepra show high levels of it. Thalidomide is expected to alleviate the symptoms of the condition by reducing the levels of TNF-alpha.

What is the stage of development of this medicine?

Thalidomide was designated as orphan medicinal product in the United States for 14 indications including erythema nodosum lepra. Marketing authorisation has been granted in the United States for erythema nodosum lepra in 1998.

Thalidomide was not marketed anywhere in the Community, at the time of submission.

At the time of submission for orphan drug status clinical trials in patients were completed.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 September 2001 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.

[*]Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition.

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	Thalidomide	Treatment of erythema nodosum leprosum (ENL) or type II lepra reactions
Bulgarian	Талидомид	Лечение на еритема нодозум лепрозум (ЕНЛ) или тип II лепра реакции.
Czech	Tahlidomid	Léčba leprózního nodozního erythému nebo leprózní reakce II. typu
Danish	Thalidomid	Behandling af erythema nodosum leprosum (ENL) eller type II leprareaktioner
Dutch	Thalidomide	Behandeling van erythema nodosum leprosum (ENL) of type-II-leprareacties
Estonian	Talidomiid	Nodoosse erüteemse leepra ja 2.tüüpi leepra reaktsioonide ravi
Finnish	*Talidomidi*	Punoittavan leprakyhmyn (ENL) hoito tai tyypin II leprareaktiot
French	Thalidomide	Traitement de l'érythème noueux lépreux (ENL) ou des réactions lépreuses de type II
German	Thalidomid	Therapie des erythema nodosum leprosum (ENL) oder Leprareaktion Typ II
Greek	ΘΑΛΙΔΟΜΙΔΗ	Θεραπεία του λεπρικού οζώδους ερυθήματος (ENL) ή των αντιδράσεων λέπρας τύπου ΙΙ.
Hungarian	Thalidomid	Leprában fellépő erythema nodosum (ENL, leprosum II-es tipusú reakciója) kezelése
Italian	Talidomide	Trattamento dell'eritema nodosum leprosum (ENL) o delle reazioni leprose di tipo II.
Latvian	Talidomīds	Eritematozas nodulāras lepras jeb II tipa lepras reakcijas ārstēšana
Lithuanian	Talidomidas	Raupsų mazginės eritemos (ENL) arba II tipo raupsų reakcijų gydymas
Maltese	Thalidomide	Kura ta' l-eritema *nodosum leprosum* (ENL) jew ta' reazzjonijiet lebbrużi tat-tip II
Polish	Talidomid	Leczenie rumienia guzowatego w przebiegu trądu lub odczynów typu II w przebiegu trądu.
Portuguese	Talidomida	Tratamento de reacções de eritema nodoso (*erythema nodosum leprosum* - ENL) ou lepra tipo II.
Romanian	Talidomidă	Tratamentul eritemului nodos lepros sau al reacţiilor leproase de tip 2
Slovak	Talidomid	Liečba erythema nodosum leprosum (ENL) alebo reakcií lepry typu II
Slovenian	Talidomid	Zdravljenje nodoznega leproznega eritema (ENL) ali leprozne reakcije tipa II
Spanish	Talidomida	Tratamiento del eritema nodoso de la lepra (ENL) o reacciones lepromatosas de tipo II.

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Swedish	*Thalidomid*	Behandling av erythema nodosum leprosum (ENL) eller typ II leprareaktioner