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EMA/COMP/733137/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Exisulind for the treatment of familial cerebral cavernous malformations

On 16 December 2014, orphan designation (EU/3/14/1387) was granted by the European Commission to Firc Institute of Molecular Oncology (IFOM), Italy, for exisulind for the treatment of familial cerebral cavernous malformations.

What are familial cerebral cavernous malformations?

Familial cerebral cavernous malformations is an inherited condition caused by mutations (defects) in certain genes that control the way that blood vessels grow. As a result of these defects, the network of blood vessels inside the brain and spinal cord develops abnormalities, with thin, fragile walls that can leak or bleed, causing damage to surrounding brain tissue and possible stroke. Some patients do not have symptoms, but the condition can result in seizures (fits), headache, weakness of arms or legs, impaired vision, and problems with memory and attention.

Familial cerebral cavernous malformations is a debilitating condition that is long lasting and may be life threatening due to severe bleeding inside the brain.

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

At the time of designation, familial cerebral cavernous malformations affected not more than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 153,000 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 application, no satisfactory methods were authorised in the EU for the treatment of familial cerebral cavernous malformations. Patients were given treatment as required for symptoms such as seizures. Some patients with symptoms were able to have surgery to remove the abnormal blood vessels.

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

How is this medicine expected to work?

The growth of abnormal blood vessels in patients with familial cerebral cavernous malformations is thought to be related to excess production of a substance called beta-catenin inside the cells lining the blood vessel walls. The active substance in the medicine, exisulind, blocks the action of an enzyme in the body called phosphodiesterase type 5 (PDE5), which is involved in the processes that stimulate the production of beta-catenin. By blocking the action of PDE5, the medicine is expected to reduce the production of beta-catenin and so lead to a reduction in the formation of abnormal blood vessels.

Exisulind is a metabolite (a by-product) of another medicine, sulindac, which has been available in the EU as an anti-inflammatory medicine since the 1970s.

What is the stage of development of this medicine?

The effects of exisulind have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with exisulind in patients with familial cerebral cavernous malformations had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for familial cerebral cavernous malformations 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 13 November 2014 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:

Firc Institute of Molecular Oncology (IFOM)
Via Adamello 16
20139 Milano
Italy
Tel. +39 02 57 43 03 234
Fax +39 02 57 43 03 23
E-mail: elisabetta.dejana@ifom.eu

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	Exisulind	Treatment of familial cerebral cavernous malformations
Bulgarian	Екзисулинд	Лечение на фамилни церебрални кавернозни малформации
Croatian	Eksisulind	Liječenje obiteljskog tipa cerebralnih kavernoznih malformacija
Czech	Exisulind	Léčba familiární mozkových kavernózní malformací
Danish	Exisulind	Behandling af familiær cerebral cavernous misdannelser
Dutch	Exisulind	Behandeling van familiale cerebraal caverneuze malformaties
Estonian	Eksisulind	Perekondliku aju kavernoossete väärarengute ravi
Finnish	Eksisulindia	Aivoverisuonten suvuttaisen ontelomuodostumia aiheuttavan kehityshäiriön hoito
French	Exisulind	Traitement des malformations familiales cérébraux caverneuses
German	Exisulind	Behandlung von familiären zerebralen kavernösen Fehlbildungen
Greek	Εξισουλίνδη	Θεραπεία των οικογενώνεγκεφαλικών σηραγγωδών δυσπλασιώ v
Hungarian	Exiszulind	Familiásis agyi cavernosus fejlődési rendellenesség kezelése
Italian	Exisulind	Trattamento delle malformazioni cavernose cerebrali familiari
Latvian	Eksisulinds	Iedzimtu cerebrālu kavernozu malformāciju ārstēšana
Lithuanian	Eksisulindas	Šeiminių smegenų kaverninių malformacijų gydymas
Maltese	Exisulind	Kura ta' deformazzjonijiet kavernużi (fil-kapillari) tal-moħħ li jintirtu
Polish	Eksisulind	Leczenie rodzinnych naczyniaków jamistych mózgu
Portuguese	Exisulind	Tratamento da malformação cavernosa cerebral familiar
Romanian	Exisulind	Tratamentul familiale cerebrale cavernos malformații
Slovak	Exisulind	Liečba familiárnych mozgových kavernóznych malformácií
Slovenian	Exisulind	Zdravljenje familiarne možganske kavernozne malformacije
Spanish	Exisulind	Tratamiento de familiares cerebrales cavernosos malformaciones
Swedish	Exisulind	Behandling av familjär cerebral cavernous missbildningar
Norwegian	Eksisulind	Behandling av familiær cerebral kavernøse malformasjoner
Icelandic	Exisúlind	Meðferð ættgengur heila holu vansköpunar

[1] At the time of designation