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EMA/COMP/216967/2012
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamide for the treatment of neurofibromatosis type 2

On 26 April 2012, orphan designation (EU/3/12/993) was granted by the European Commission to Sirius Regulatory Consulting Limited, United Kingdom, for N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamide for the treatment of neurofibromatosis type 2.

What is neurofibromatosis type 2?

Neurofibromatosis type 2 is an inherited disease in which the patient develops benign (noncancerous) tumours in the nervous system, most commonly along the acoustic nerve that carries signals from the ear to the brain. Symptoms include hearing loss, tinnitus (ringing or buzzing in the ears), problems with balance, headache, numbness and weakness. Patients may also have lesions in the eyes and skin.

The disease is caused by mutations (defects) in a gene called NF2, which plays a role in preventing cells from dividing uncontrollably.

Neurofibromatosis type 2 is a debilitating disease due to the damage caused by the tumours, particularly to hearing and balance. Tumours can also be life-threatening due to the risk of them becoming cancerous or interfering with vital body functions.

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

At the time of designation, neurofibromatosis type 2 affected approximately 0.17 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 8,600 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 orphan designation, no satisfactory treatments were authorised in the EU for this condition. Treatment mainly involved managing the symptoms of the disease. Surgery was commonly used to remove the tumours.

How is this medicine expected to work?

In patients with neurofibromatosis type 2, the cells in the nervous system, particularly the Schwann cells covering the acoustic nerve, divide uncontrollably, causing the formation of tumours. This medicine is expected to shrink tumours and reduce tumour formation mainly by blocking the activity of histone deacetylases (HDACs), proteins that promote cell division. By blocking HDACs, the medicine is expected to stop the tumour cells from dividing and multiplying, leading to cell death. The medicine may also work through other means such as damaging the internal skeleton of the tumour cells and blocking the ability of the cells to repair their DNA.

What is the stage of development of this medicine?

The effects of N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with neurofibromatosis type 2 had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for neurofibromatosis type 2 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 8 March 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	N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamide	Treatment of neurofibromatosis type 2
Bulgarian	N-хидрокси-4-3-метил-2-(S)-фенил-бутириламино бензамид	Лечение на неврофиброматоза тип 2
Czech	N-hydroxy-4-(3-methyl-2-(S)-fenyl-butyrylamino) benzamidu	Léčba neurofibromatózy typu 2
Danish	N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamid	Behandling af neurofibromatose type 2
Dutch	N-hydroxy-4-(3-methyl-2-(S)-fenyl-butyrylamino) benzamide	Behandeling van neurofibromatose type 2
Estonian	N-hüdroksü-4-(3-metüül-2-(S)-fenüül-butyrylamino) bensamiid	2.tüüpi neurofibromatoosi ravi
Finnish	N-hydroksi-4-(3-metyyli-2-(S)-fenyyli-butyrylamino)-bentsamidi	Tyypin 2 neurofibromatoosin hoito
French	N-hydroxy-4-(3-méthyl-2-(S)-phényl-butyrylamino) benzamide	Traitement de la neurofibromatose de type 2
German	N-Hydroxy-4-(3-methyl-2-(S)-phenyl-Butyrylamino) benzamid	Die Behandlung der Neurofibromatose-Typ-2
Greek	Ν-υδροξυ-4-(3-μεθυλο-2-(S)-φαινυλο-βουτυρυλαμινο) βενζαμίδιο	Θεραπεία της νευροϊνωμάτωσης-τύπου 2
Hungarian	N-hidroxi-4-(3-metil-2-(S)-fenil-butyrylamino) benzamid	2-es típusú neurofibromatózis kezelése
Italian	N-idrossi-4-(3-metil-2-(S)-fenil-butyrylamino) benzamide	Trattamento di neurofibromatosi di tipo 2-complesso malattia
Latvian	N-hidroksi-4-(3-metil-2-(S)-fenil-butirilamino) benzamīds	2 tipa 2 neirofibromatozes srstēšana
Lithuanian	N-hidroksi-4-(3-metil-2-(S)-fenil-butirilamino) benzamidas	Neurofibromatozės (2 tipo) gydymas
Maltese	N-hydroxy-4-(3-methyl-2-(S)-phenyl-butyrylamino) benzamide	Kura tan-newrofibromatosi tat-tip 2
Polish	N-hydroksy-4-(3-metylo-2-(S)-fenylo-butyroamino) benzamid	Leczenie nerwiakowłókniakowatości typu 2
Portuguese	N-hidroxi-4-(3-metil-2-(S)-fenil-butirilamino) benzamida	Tratamento de neurofibromatose tipo 2
Romanian	N-hidroxi-4-(3-metil-2-(S)-fenil-butirilamino) benzamidă	Tratamentul neurofibromatozei tip 2
Slovak	N-hydroxy-4-(3-metyl-2-(S)-fenyl-butyrylamino) benzamid	Liečba neurofibromatózy typu 2
Slovenian	N-hidroksi-4-(3-metil-2-(S)-fenil-butirilamino) benzamid	Zdravljenje neurofibromatoze tipa 2

[1] At the time of designation

Language	Active ingredient	Indication
Spanish	N-hidroxi-4-(3-metil-2-(S)-fenil-butirilamino) benzamida	Tratamiento de la neurofibromatosis de tipo 2
Swedish	N-hydroxi-4-(3-metyl-2-(S)-fenyl-butyrylamino) bensamid	Behandling av neurofibromatos typ 2
Norwegian	N-hydrosy-4-(3-metyl-2-(S)-fenyl-butyrylamino) benzamid	Behandling av Nevrofibromatose-type 2 sykdom komplekse
Icelandic	N-hýdroxý-4-(3-metýl-2-(S)-fenýl-bútýrýlamínó) benzamíð	Meðferð við neurofibromatosis-gerð 2