13 September 2019
EMADOC-628903358-1132

Public summary of opinion on orphan designation

N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide for the treatment of neurofibromatosis type 1

On 25 July 2019, orphan designation EU/3/19/2184 was granted by the European Commission to Voisin Consulting S.A.R.L., France, for N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide (also known as PD-0325901) for the treatment of neurofibromatosis type 1.

What is neurofibromatosis type 1?

Neurofibromatosis type 1 is an inherited disease in which the patient develops benign (non-cancerous) tumours along the nerves. The severity of the disease varies from patient to patient, and symptoms include pale, coffee-coloured patches, freckles in unusual places (such as the armpits, groin and under the breasts), high blood pressure, problems with the bones, eyes and nervous system, learning difficulty and short stature. Patients can also develop cancer, including cancer of the optic nerve (the nerve that sends signals from the eye to the brain).

The disease is caused by mutations (changes) in a gene called NF1, which leads to uncontrolled growth of cells in the nervous system.

Neurofibromatosis type 1 is a debilitating disease because of the damage caused by the tumours. The disease may also be life threatening due to the increased risk of developing cancer.

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

At the time of designation, neurofibromatosis type 1 affected approximately 3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 156,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What treatments are available?

At the time of designation, there were no treatments authorised in the EU for neurofibromatosis type 1. Surgery was used to remove tumours, and chemotherapy (medicines for treating cancer) was used for cancers caused by the condition.

How is this medicine expected to work?

This medicine blocks enzymes called MEK1/2 which are involved in stimulating cells to grow. MEK1/2 are overactive in certain types of cancer, which makes cells grow uncontrollably. By blocking these enzymes, the medicine is expected to slow down growth of the tumour cells in neurofibromatosis type 1.

What is the stage of development of this medicine?

The effects of N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide 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 neurofibromatosis type 1 were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of neurofibromatosis type 1. Orphan designation for this medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 20 June 2019, 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.

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:

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide	Treatment of neurofibromatosis type 1
Bulgarian	N-((R)-2,3-дихидроксипропоксил)-3,4-дифлуро-2-(2-флуоро-4-йодо-фениламино)-бензамид	Лечение на неврофиброматоза тип 1
Croatian	N-((R)-2,3-dihidrokspropoksil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamid	Liječenje neurofibromatoze tipa 1
Czech	N-((2R)-2,3-dihydroxypropoxy)-3,4-difluor-2-(2-fluor-4-jodfenylamino)benzamid	Léčba neurofibromatózy typu 1
Danish	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamid	Behandling af neurofibromastosis type 1
Dutch	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamide	Behandeling van neurofibromatosis type 1
Estonian	N-((R)-2,3-dihüdroksüpropoksüül)-3,4-difluoro-2-(2-fluoro-4-iodo-fenüülamino)-bensamiid	1. tüüpi neurofibromatoosi ravi
Finnish	N-((R)-2,3-dihydroksipropoksyyli)-3,4-difluro-2-(2-fluoro-4-jodi-fenyyliamino)-bentsamidi	Tyypin 1 neurofibromatoosin hoito
French	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phénylamino)-benzamide	Traitement de la neurofibromatose de type 1
German	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-phenylamino)-benzamid	Behandlung der Neurofibromastose Typ 1
Greek	N-((R)-2,3-διυδροξυπροποξυλ)-3,4-διφθορο-2-(2-φθορο-4-ιωδο-φαινυλαμινο)-βενζαμίδιο	Θεραπεία της νευροϊνομάτωσης τύπου Ι
Hungarian	N-((R)-2,3-dihidroxipropoxil)-3,4-difluro-2-(2-fluoro-4-jodo-fenilamino)-benzamid	1-es típusú neurofibromatozis kezelése
Italian	N-((R)-2,3-diidrossipropossil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamide	Trattamento della neurofibromatosi tipo 1
Latvian	N-((R)-2,3-dihidroksipropoksil)-3,4-difluro-2-(2-fluoro-4-jodo-fenilamino)-benzamīds	1. tipa neirofibromatozes ārstēšana
Lithuanian	N-((R)-2,3-dihidroksipropoksil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamidas	Neurofibromatozės I tipo gydymas
Maltese	N-((R)-2,3-diidrossipropossil)-3,4-difluro-2-(2-fluworo-4-jodo-fenilammino)-benżammid	Kura ta' newrofibromatożi tat-tip 1
Polish	N-((R)-2,3-dihydroksypropoksylo)-3,4-difluro-2-(2-fluoro-4-jodo-fenylamino)-benzamid	Leczenie nerwiakowłókniakowatości typu 1

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	N-((R)-2,3-di-hidroxipropoxil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamida	Tratamento da neurofibromatose de tipo 1
Romanian	N-((R)-2,3-di-hidroxipropoxil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamidă	Tratamentul neurofibromatozei de tip 1
Slovak	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-jodo-fenylamino)-benzamid	Liečba neurofibromatózy typu 1
Slovenian	N-((R)-2,3-dihidroksipropoksil)-3,4-difluoro-2-(2-fluoro-4-iodo-fenilamino)-benzamid	Zdravljenje nevrofibromatoze tipa1
Spanish	N-((R)-2,3-dihidroxipropoxil)-3,4-difluro-2-(2-fluoro-4-iodo-fenilamino)-benzamide	Tratamiento de la neurofibromatosis de tipo 1
Swedish	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-fenylamino)-benzamid	Behandling av neurofibromastos typ 1
Norwegian	N-((R)-2,3-dihydroksypropoksyl)-3,4-difluoro-2-(2-fluoro-4-jodo-fenylamino)-benzamid	Behandling av nevrofibromatose type 1
Icelandic	N-((R)-2,3-dihydroxypropoxyl)-3,4-difluro-2-(2-fluoro-4-iodo-fenýlamínó)-benzamíð	Meðferð við taugatrefjaæxlageri af tegund 1