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Public summary of opinion on orphan designation

(2S,3R,4R,5S)-2-(Hydroxymethyl)-1-pentylpiperidine-3,4,5-triol for the treatment of GM2 gangliosidosis

On 13 November 2019, orphan designation EU/3/19/2218 was granted by the European Commission to Idorsia Pharmaceuticals Deutschland GmbH, Germany, for (2S,3R,4R,5S)-2-(hydroxymethyl)-1-pentylpiperidine-3,4,5-triol (also known as ACT-519276) for the treatment of GM2 gangliosidosis.

What is GM2 gangliosidosis?

GM2 gangliosidosis is an inherited disorder that causes progressive damage to the nerve cells in the brain and spinal cord.

Patients with this condition lack an enzyme called beta-hexosaminidase, which normally breaks down substances called GM2 gangliosides. Without this enzyme, GM2 gangliosides build up in the body, particularly in the brain and spinal cord. The condition causes muscle weakness, problems with walking, intellectual disability, difficulty speaking, seizures (fits), and loss of sight and hearing.

GM2 gangliosidosis is a debilitating and life-threatening disease. The most severe form of the disease starts in early infancy and can lead to death during childhood.

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

At the time of designation, GM2 gangliosidosis affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 21,000 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 designation, no satisfactory methods were authorised in the EU to treat GM2 gangliosidosis. Treatment of patients was mainly supportive and included physical therapy and medicines to manage symptoms such as seizures.

*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).

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How is this medicine expected to work?

The medicine, which can be given by mouth, blocks the effects of two enzymes that are important for the formation of GM2 gangliosides. The medicine is expected to enter the brain and reduce the production and build-up of GM2 gangliosides and thereby slow down the progression of GM2 gangliosidosis and help patients live longer.

What is the stage of development of this medicine?

The effects of the medicine 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 GM2 gangliosidosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of GM2 gangliosidosis or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 10 October 2019, 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:

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	(2S,3R,4R,5S)-2-(hydroxymethyl)-1-pentylpiperidine-3,4,5-triol	Treatment of GM2 gangliosidosis
Bulgarian	(2S,3R,4R,5S)-2-(хидроксиметил)-1-пентилпиперидин-3,4,5-триол	Лечение на GM2 ганглиозидоза
Croatian	(2S,3R,4R,5S)-2-(hidroksimetil)-1-pentilpiperidin-3,4,5-triol	Liječenje GM2 gangliozidoze
Czech	(2S,3R,4R,5S)-2-(hydroxymethyl)-1-pentylpiperidin-3,4,5-triol	Léčba GM2 gangliosidozy
Danish	(2S,3R,4R,5S)-2-(hydroxymethyl)-1-pentylpiperidin-3,4,5-triol	Behandling af GM2 gangliosidosis
Dutch	(2S,3R,4R,5S)-2-(hydroxymethyl)-1-pentylpiperidine-3,4,5-triol	Behandeling vanGM2 gangliosidose
Estonian	(2S,3R,4R,5S)-2-(hüdroksümetüül)-1-pentüülpiperidiin-3,4,5-triool	GM2 gangliosidoosi ravi
Finnish	(2S,3R,4R,5S)-2-(hydroksimetyyli)-1-pentyylipiperidiini-3,4,5-trioli	GM2-gangliosidoosin hoito
French	(2S,3R,4R,5S)-2-(hydroxyméthyle)-1-pentylpipéridine-3,4,5-triol	Traitement de la gangliosidose à GM2
German	(2S,3R,4R,5S)-2-(Hydroxymethyl)-1-pentylpiperidin-3,4,5-triol	Behandlung der GM2 Gangliosidose
Greek	(2S,3R,4R,5S)-2-(υδροξυμεθυλο)-1-πεντυλοπιπεριδινο-3,4,5-τριόλη	Θεραπεία της γαγγλιοσίδοσης GM2
Hungarian	(2S,3R,4R,5S)-2-(hidroximetil)-1-pentil-piperidin-3,4,5-triol	GM2 gangliozidózis kezelése
Italian	(2S,3R,4R,5S)-2-(idrossimetil)-1-pentilpiperidina-3,4,5-triolo	Trattamento della gangliosidosi GM2
Latvian	(2S,3R,4R,5S)-2-(hidroksimetil)-1-pentilpiperidīn-3,4,5-triols	GM2 gangliozidozes ārstēšana
Lithuanian	(2S,3R,4R,5S)-2-(hidroksimetil)-1-pentilpiperidino-3,4,5-triolis	GM2 gangliozidozės gydymas
Maltese	(2S,3R,4R,5S)-2-(idrossimetil)-1-pentilpiperidina-3,4,5-trijol	Kura ta’ ganglijosidoži GM2

[1] At the time of designation

Language	Active ingredient	Indication
Polish	(2S,3R,4R,5S)-2-(hydroksymetylo)-1-pentylopiperydyno-3,4,5-triol	Leczenie gangliozydozy GM2
Portuguese	(2S,3R,4R,5S)-2-(hidroximetil)-1-pentilpiperidina-3,4,5-triol	Tratamento da gangliosidose GM2
Romanian	(2S,3R,4R,5S)-2-(hidroximetil)-1-pentilpiperidin-3,4,5-triol	Tratamentul gangliozidozei GM2
Slovak	(2S,3R,4R,5S)-2-(hydroxymetyl)-1-pentylpiperidín-3,4,5-triol	Liečba GM2 gangliozidózy
Slovenian	(2S,3R,4R,5S)-2-(hidroksimetil)-1-pentilpiperidin-3,4,5-triol	Zdravljenje GM2 gangliozidoze
Spanish	(2S,3R,4R,5S)-2-(hidroximetil)-1-pentilpiperidina-3,4,5-triol	Tratamiento de Gangliosidosis GM2
Swedish	(2S,3R,4R,5S)-2-(hydroximetyl)-1-pentylpiperidin-3,4,5-triol	Behandling av GM2-gangliosidos
Norwegian	(2S,3R,4R,5S)-2-(hydroksymetyl)-1-pentylpiperidin-3,4,5-triol	Behandling av GM2 gangliosidose
Icelandic	(2S,3R,4R,5S)-2-(hýdroxýmetýl)-1-pentýlpíperidín-3,4,5-tríól	Meðferð á GM2 ganglíósídósis