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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Melatonin for the treatment of Smith-Magenis syndrome

On 14 October 2016, orphan designation (EU/3/16/1755) was granted by the European Commission to Therapicon Srl, Italy, for the melatonin for the treatment of Smith-Magenis syndrome.

What is Smith-Magenis syndrome?

Smith-Magenis syndrome is a disorder with a variety of features including intellectual disability, speech and language delay, distinctive facial features, difficulty sleeping and behavioural problems. In some patients, organ malformations are present, affecting mostly the heart and kidneys. The severity of the disorder varies from one person to another.

The disorder is caused by the loss or damage of a gene called *retinoic acid-induced 1*. This genetic abnormality is not inherited from the parents but seems to occur spontaneously.

Smith-Magenis syndrome is a long-term debilitating disease because it causes intellectual disability and behavioural problems.

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

At the time of designation, Smith-Magenis syndrome affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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 medicines were authorised in the EU for the treatment of Smith-Magenis syndrome. Patients were given general support, such as behavioural and speech therapy.

*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 513,700,000 (Eurostat 2016).

How is this medicine expected to work?

Melatonin is a natural hormone that helps encourage and regulate sleep. Patients with Smith-Magenis syndrome have difficulty sleeping at night but are sleepy during the day. This is because their levels of melatonin reach their peak during the day, instead of the middle of the night.

By giving additional melatonin at night its levels can be increased, helping patients to sleep. This is combined with another medicine, acebutolol hydrochloride given in the morning, which is expected to help patients stay awake during the day. In this way, the two medicines would help to normalise the sleep cycle of patients with Smith-Magenis syndrome.

What is the stage of development of this medicine?

The sponsor has provided data from the published literature to support its application for orphan designation.

At the time of submission of the application for orphan designation, no clinical trials with melatonin in patients with Smith-Magenis syndrome had been started.

At the time of submission, melatonin was not authorised anywhere in the EU for Smith-Magenis syndrome 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 September 2016 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, on the medicine's [rare disease designations page](#).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Melatonin	Treatment of Smith-Magenis syndrome
Bulgarian	Мелатонин	лечение на синдрома на Смит-Мадженис
Croatian	Melatonin	Liječenje Smith-Magenisovog sindroma
Czech	Melatonin	Léčba Smith-Magenis syndromu
Danish	Melatonin	Behandling af Smith-Magenis syndrom
Dutch	Melatonine	Behandeling van Smith-Magenis syndroom
Estonian	Melatoniin	Smith-Magenis sündroomi ravi
Finnish	Melatonini	Smith-Magenisin oireyhtymän hoito
French	Mélatonine	Traitement du syndrome de Smith-Magenis
German	Melatonin	Behandlung des Smith-MagenisSyndroms
Greek	Μελατονίνη	Θεραπεία του συνδρόμου Smith-Magenis
Hungarian	Melatonin	Smith-Magenis-szindróma kezeléské
Italian	Melatonina	Trattamento della sindrome di Smith-Magenis
Latvian	Melatonīns	Smita-Magenisa (<i>Smith-Magenis</i>) sindroma ārstēšana
Lithuanian	Melatoninas	<i>Smith-Magenis</i> sindromo gydymas
Maltese	Melatonina	Kura tas-sindrome ta' Smith-Magenis
Polish	Melatonina	Leczenia zespołu Smith-Magenis
Portuguese	Melatonina	Tratamento da síndrome de Smith-Magenis
Romanian	Melatonină	Tratamentul sindromului Smith-Magenis
Slovak	Melatonín	Liečba Smith-Magenis syndrómu
Slovenian	Melatonin	Zadavljenje Smith-Magenis sindroma
Spanish	Melatonina	Tratamiento del síndrome de Smith-Magenis
Swedish	Melatonin	Behandlingen av Smith-Magenis syndrom
Norwegian	Melatonin	Behandling av Smith-Magenis syndrom
Icelandic	Melatónín	Meðferð við Smith-Magenisheilkenni

¹ At the time of designation