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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Acebutolol hydrochloride for the treatment of Smith-Magenis syndrome

On 14 October 2016, orphan designation (EU/3/16/1742) was granted by the European Commission to Therapicon Srl, Italy, for acebutolol hydrochloride 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).

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How is this medicine expected to work?

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

Acebutolol hydrochloride works by decreasing the release of natural melatonin. It is intended to be given in the morning, which is expected to reduce the melatonin peak during the day and help patients stay awake. Patients would then be given melatonin at night to help them to sleep. 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 acebutolol hydrochloride in patients with Smith-Magenis syndrome had been started.

Acebutolol hydrochloride is a medicine known as beta blocker which has been used for many years for treating high blood pressure.

At the time of submission, acebutolol hydrochloride 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.

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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, 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Acebutolol hydrochloride	Treatment of Smith-Magenis syndrome
Bulgarian	Ацебутолол хидрохлорид	лечение на синдрома на Смит-Маджениc
Croatian	Acebutolol hidroklorid	Liječenje Smith-Magenisovog sindroma
Czech	Acebutolol hydrochlorid	Léčba Smith-Magenis syndromu
Danish	Acebutolol hydrochlorid	Behandling af Smith-Magenis syndrom
Dutch	Acebutolol hydrochloride	Behandeling van Smith-Magenis syndroom
Estonian	Atsebutoloolvesinikkloriid	Smith-Magenis sündroomi ravi
Finnish	Asebutololihydrokloridi	Smith-Magenisin oireyhtymän hoito
French	Acébutolol chlorhydrate	Traitement du syndrome de Smith-Magenis
German	Acebutolol Hydrochlorid	Behandlung des Smith-MageniscSyndroms
Greek	Ακεβουτολόλη υδροχλωρικη	Θεραπεία του συνδρόμου Smith-Magenis
Hungarian	Acebutolol hidroklorid	Smith-Magenis-szindróma kezelésére
Italian	Acebutololo cloridrato	Trattamento della sindrome di Smith-Magenis
Latvian	Acebutolola hidrohlorīds	Smita-Magenisa (*Smith-Magenis*) sindroma ārstēšana
Lithuanian	Acebutololio hidrochloridas	*Smith-Magenis* sindromo gydymas
Maltese	Acebutolol hydrochloride	Kura tas-sindrome ta' Smith-Magenis
Polish	Chlorowodorek acebutololu	Leczenie zespołu Smith-Magenis
Portuguese	Acebutolol cloridrato	Tratamento da síndrome de Smith-Magenis
Romanian	Acebutolol clorhidrat	Tratamentul sindromului Smith-Magenis
Slovak	Acebutolol hydrochlorid	Liečba Smith-Magenis syndrómu
Slovenian	Acebutolol hidroklorid	Zadravljenje Smith-Magenis sindroma
Spanish	clorhidrato de Acebutolol	Tratamiento del síndrome de Smith-Magenis
Swedish	Acebutolol hydroklorid	Behandlingen av Smith-Magenis syndrom
Norwegian	Acebutolol hydrokloride	Behandling av Smith-Magenis syndrom
Icelandic	Acebútólól hýdróklóríð	Meðferð við Smith-Magenis-heilkenni

[1] At the time of designation