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EMA/COMP/552875/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Osilodrostat for the treatment of Cushing's syndrome

On 15 October 2014, orphan designation (EU/3/14/1345) was granted by the European Commission to Novartis Europharm Ltd, United Kingdom, for osilodrostat for the treatment of Cushing's syndrome.

What is Cushing's syndrome?

Cushing's syndrome is a disease characterised by an excess of the hormone cortisol in the blood. It is usually caused by a tumour of the pituitary gland (a gland located at the base of the brain) that produces large amounts of adrenocorticotropic hormone (ACTH), which in turn stimulates the production of excess cortisol from the adrenal glands, which are situated above the kidney. Some patients with the syndrome have other kinds of tumours that produce ACTH, or tumours that produce excess cortisol directly.

Symptoms of Cushing's syndrome include weight gain affecting the face and torso but not the limbs, growth of fat above the collar bone and the back of the neck, a roundish face, easy bruising, excessive growth of coarse hair on the face, weakening of the muscles and bones, depression, diabetes and high blood pressure.

Cushing's syndrome is a severe disease that is long lasting and may be life threatening because of its complications, including diabetes, high blood pressure and mental problems.

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

At the time of designation, Cushing's 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).

*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 511,100,000 (Eurostat 2014).

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What treatments are available?

At the time of designation, the main treatment for ACTH-dependent Cushing's syndrome involved surgery to remove the tumour responsible for causing the high cortisol levels, sometimes followed by radiotherapy (treatment with radiation). Several medicines were authorised in the EU to reduce the production of cortisol, including aminoglutethimide, metyrapone, mitotane and pasireotide.

The sponsor has provided sufficient information to show that osilodrostat might be of significant benefit for patients with Cushing's syndrome because early results in patients with Cushing's syndrome show that osilodrostat has a significant effect in normalising cortisol levels. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The symptoms of Cushing's syndrome are due to the production of excess amounts of cortisol in the body, a process that requires an enzyme called 11-beta-hydroxylase. Osilodrostat blocks the action of this enzyme, reducing the production of cortisol and lowering the level of the hormone in the body. This is expected to reduce the complications of the condition.

What is the stage of development of this medicine?

The effects of osilodrostat have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with osilodrostat in patients with Cushing's syndrome due to tumours of the pituitary gland were ongoing.

At the time of submission, osilodrostat was not authorised anywhere in the EU for treatment of Cushing's syndrome. Orphan designation of the medicine had been granted in the United States for treatment of Cushing's disease (Cushing's syndrome due to a tumour of the pituitary gland).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 September 2014 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	Osilodrostat	Treatment of Cushing's syndrome
Bulgarian	Осилодростат	Лечение на синдром на Кушинг
Croatian	Osilodrostat	Liječenje Cushingovog sindroma
Czech	Osilodrostat	Léčba Cushingova syndromu
Danish	Osilodrostat	Behandling af Cushings syndrom
Dutch	Osilodrostat	Behandeling van Cushing syndroom
Estonian	Osilodrostaat	Cushingi sündroomi ravi
Finnish	Osilodrostaatti	Cushingin oireyhtymän hoito
French	Osilodrostat	Traitement du syndrome de Cushing
German	Osilodrostat	Behandlung des Cushing-Syndroms
Greek	Οσιλοδροστάτη	Θεραπεία του συνδρόμου Cushing
Hungarian	Ozilodrosztat	A Cushing-szindróma kezelése
Italian	Osilodrostat	Trattamento della sindrome di Cushing
Latvian	Osilodrostats	Kušinga sindroma ārstēšana
Lithuanian	Osilodrostatas	Kušingo (Cushing) sindromo gydymas
Maltese	Osilodrostat	Kura tas-sindromu ta' Cushing
Polish	Osylodrostat	Leczenie zespołu Cushinga
Portuguese	Osilodrostato	Tratamento da síndrome de Cushing
Romanian	Osilodrostat	Tratamentul sindromului Cushing
Slovak	Osilodrostat	Liečba Cushingovho syndrómu
Slovenian	Osilodrostat	Zdravljenje Cushingovega sindroma
Spanish	Osilodrostat	Tratamiento del síndrome de Cushing
Swedish	Osilodrostat	Behandling av Cushings syndrom
Norwegian	Osilodrostat	Behandling av Cushings syndrom
Icelandic	Ósílódróstat	Meðferð við Cushingsheilkenni

[1] At the time of designation