8 March 2018
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Public summary of opinion on orphan designation

N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino)phenyl]cyclopentyl]methyl]urea, hydrochloride salt for the treatment of congenital adrenal hyperplasia

On 17 January 2018, orphan designation (EU/3/17/1967) was granted by the European Commission to Millendo Therapeutics Ltd, United Kingdom, for N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino)phenyl]cyclopentyl]methyl]urea, hydrochloride salt (also known as ATR-101) for the treatment of congenital adrenal hyperplasia.

What is congenital adrenal hyperplasia?

Congenital adrenal hyperplasia is a group of inherited conditions where patients are unable to produce normal amounts of the steroid hormones cortisol and aldosterone. These hormones play an important role in responding to stress and regulating salt and water in the body. The hormones are produced by the adrenal glands, two small glands that are located above the kidneys. In patients with the condition, the adrenal glands produce male sex hormones instead of cortisol and aldosterone. Congenital adrenal hyperplasia can be caused by many different mutations (changes) in the genes controlling the production of cortisol and aldosterone.

Congenital adrenal hyperplasia is long-term debilitating and life-threatening condition due to a failure of the response to stress (adrenal insufficiency), altered amounts of salt and water in the body, low blood pressure, and early puberty in boys or development of masculine characteristics in girls, which can lead to growth stopping early and short stature.

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

At the time of designation, congenital adrenal hyperplasia affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 52,000 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 515,700,000 (Eurostat 2017).

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What treatments are available?

At time of designation, several products to treat congenital adrenal hyperplasia were authorised in the EU. In particular, various steroid hormones were used to replace those which are insufficiently produced by the adrenal gland and to control the production of excess male sex hormones.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with congenital adrenal hyperplasia because early data show that it reduces the levels of substances the body uses to produce male sex hormones. 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?

This medicine blocks an enzyme called ACAT1, which is involved in the production of male sex hormones. As an increase in male sex hormones is one of the effects of the disease, the medicine is expected to reduce some of the symptoms.

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, clinical trials with the medicine in patients with congenital adrenal hyperplasia were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital adrenal hyperplasia. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 December 2017 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	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino)phenyl]cyclopentyl]methyl]urea, hydrochloride salt	Treatment of congenital adrenal hyperplasia
Bulgarian	N-[2,6-бис(1-метилетил)фенил]-N'-[[1-[4-(диметиламино)фенил] циклопентил]метил]урея, хидрохлорид	Лечение на вродена надбъбречна хиперплазия
Croatian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urea, hidrokloridna sol	Liječenje kongenitalne adrenalne hiperplazije
Czech	N-[2,6-bis(1-methylethyl)fenyl]-N'-[[1-[4-(dimethylamino) fenyl]cyklopentyl]methyl]močovina, hydrochloridová sůl	Léčba vrozené hyperplasie nadledvin
Danish	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]urea, hydrochloridsalt	Behandling af medfødt binyrebarkhyperplasi
Dutch	N-[2,6-bis(1-methylethyl)fenyl]-N'-[[1-[4-(dimethylamino) fenyl]cyclopentyl]methyl]ureum, hydrochloridezout	Behandeling van congenitale bijnierhyperplasia
Estonian	N-[2,6-bis(1-metüületüül)fenüül]-N'-[[1-[4-(dimetüülamino) fenüül]tsüklopentüül]metüül]uurea hüdrokloriidsool	Kaasasündinud neerupealise hüperplaasia ravi
Finnish	N-[2,6-bis(1-metyylietyyli)fenyyli]-N'-[[1-[4-(dimetyyliamino) fenyyli]syklopentyyli]metyyli]urea, hydrokloridisuola	Lisämunuaisen synnynnäisen liikakasvun hoito
French	Sel chlorhydrate de N-[2,6-bis(1-méthyléthyl)phényl]-N'-[[1-[4-(diméthylamino) phényl]cyclopentyl]méthyl]urée	Traitmement de l'hyperplasie surrénale congénitale
German	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]Harnstoff, Hydrochloridsalz	Behandlung der Kongenitalen Adrenalen Hyperplasie
Greek	N-[2,6-δι(1-μεθυλαιθυλ)φαινυλο]-N'-[[1-[4-(διμεθυλαμινο) φαινυλο]κυκλοπεντυλ]μεθυλ]ουρία, υδροχλωρικό άλας	Θεραπεία της συγγενούς επινεφριδιακής υπερπλασίας
Hungarian	N-[2,6-bisz(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urea, hidroklorid só	Congenitalis adrenalis hyperplasia kezelése
Italian	N-[2,6-bis(1-metil-etil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil]urea, sale cloridrato	Trattamento dell'iperplasia surrenale congenita

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino)fenil]ciklopentil]metil]urīnvielas hidrohlorīda sāls	Iedzimtas virsnieru hiperplāzijas ārstēšana
Lithuanian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]šlapalas, hidrochlorido druska	Įgimtos antinksčių hiperplazijos gydymas
Maltese	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ċiklopentil]metil]urea, melħ idrokloridu	Kura ta' l-iperplasija adrenali konġenitali
Polish	Chlorowodorek N-[2,6-bis(1-metyloetylo)fenylo]-N'-[[1-[4-(dimetyloamino) fenylo]cyklopentylo]metylo]mocznika	Leczenie wrodzonego przerostu nadnerczy
Portuguese	Cloridrato de *N*-[2,6-bis(1-metiletil)fenil]-*N*'-[[1-[4-(dimetilamino)fenil]ciclopentil]metil]ureia	Tratamento da hiperplasia adrenal congenita
Romanian	Clorhidrat de N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil]uree	Tratamentul hiperplaziei congenitale corticosuprarenale
Slovak	N-[2,6-bis(1-metyletyl)fenyl]-N'-[[1-[4-(dimetylamino) fenyl]cyklopentyl]metyl]urea, soľ kyseliny chlorovodíkovej	Liečba kongenitálnej nadobličkovej hyperplázie
Slovenian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urea, hidrokloridna sol	Kongenitalna adrenalna hiperplazija
Spanish	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil]urea, sal clorhidrato	Tratamiento de la hiperplasia suprarrenal congénita
Swedish	N-[2,6-bis(1-metyletyl)fenyl]-N'-[[1-[4-(dimetylamino) fenyl]cyklopentyl]metyl]urea, hydrokloridsalt	Behandling av adrenogenitalt syndrom
Norwegian	N-[2,6-bis(1-metyletyl)fenyl]-N'-[[1-[4-(dimetylamino)fenyl]syklopentyl]metyl]urea, hydrokloridsalt	Behandling av kongenitt binyrebarkhyperplasi
Icelandic	N-[2,6-bis(1-metýletýl)fenýl]-N'-[[1-[4-(dímetýlamínó) fenýl]cýklópentýl]metýl]úrea, hýdróklóríðsalt	Meðfædd nýrnahettu hyperplasía