18 June 2013
EMA/COMP/277098/2013
Committee for Orphan Medicinal Products

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 adrenocortical carcinoma

On 7 June 2013, orphan designation (EU/3/13/1128) was granted by the European Commission to Atterocor Ltd, United Kingdom, for N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]urea, hydrochloride salt for the treatment of adrenocortical carcinoma.

What is adrenocortical carcinoma?

Adrenocortical carcinoma is a cancer of the adrenal cortex, which is the outside layer of the adrenal glands, small glands located above the kidneys. The adrenal cortex produces several steroid hormones, including sex hormones (which cause the body to have masculine or feminine characteristics), aldosterone (which helps to regulate the body's blood pressure) and cortisol (also known as the stress hormone because it is released in response to stress). In adrenocortical carcinoma too much of one or more of these steroid hormones is produced. Symptoms associated with adrenocortical carcinoma may include weakening of the muscles and bones, high blood pressure and the development of abnormal masculine or feminine features if the sex hormones are affected.

Adrenocortical carcinoma is a life-threatening disease with overall survival ranging between 13 and 30 months.

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

At the time of designation, adrenocortical carcinoma affected approximately 0.09 in 10,000 people in the European Union (EU). This was equivalent to a total of around 5,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

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What treatments are available?

At the time of designation, the main treatment for adrenocortical carcinoma was surgery together with chemotherapy (medicines to treat cancer), while radiotherapy was also sometimes used. Mitotane was authorised in the EU for use with other anticancer medicines to treat adrenocortical carcinoma.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with adrenocortical carcinoma because it works in a different way to existing treatments and early studies in experimental models show that it may shrink the tumour. This assumption of significant benefit 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 exact way the medicine works against cancer cells is not known, but the medicine has been shown to block an enzyme called 'acyl-coA:cholesterol acyltransferase', which is found in the cells of the adrenal cortex and is needed for the normal function of these cells.

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 adrenocortical carcinoma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of adrenocortical carcinoma. Orphan designation of the medicine had been granted for the condition in the United States of America.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 17 April 2013 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	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]urea, hydrochloride salt	Treatment of adrenocortical carcinoma
Bulgarian	N-[2,6-бис(1-метилетил)фенил]-N'-[[1-[4-(диметиламино)фенил] циклопентил]метил]урея, хидрохлорид	Лечение на адренокортикален карцином
Czech	N-[2,6-bis(1-methylethyl)fenyl]-N'-[[1-[4-(dimethylamino) fenyl]cyklopentyl]methyl]močovina, hydrochloridová sůl	Léčba non-dystrofické myotonie
Danish	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]urea, hydrochloridsalt	Behandling af adrenokortikalt karcinom
Dutch	N-[2,6-bis(1-methylethyl)fenyl]-N'-[[1-[4-(dimethylamino) fenyl]cyclopentyl]methyl]ureum, hydrochloridezout	Behandeling van bijnierschorscarcinoom
Estonian	N-[2,6-bis(1-metüületüül)fenüül]-N'-[[1-[4-(dimetüülamino) fenüül]tsüklopentüül]metüül]uurea hüdrokloriidsool	Neerupealise koore kartsinoomi ravi
Finnish	N-[2,6-bis(1-metyylietyyli)fenyyli]-N'-[[1-[4-(dimetyyliamino) fenyyli]syklopentyyli]metyyli]urean hydrokloridisuola	Lisämunuaisen kuorikerroksen karsinooman hoitoon
French	Sel chlorhydrate de N-[2,6-bis(1-méthyléthyl)phényl]-N'-[[1-[4-(diméthylamino) phényl]cyclopentyl]méthyl]urée	Traitement du carcinome corticosurrénalien
German	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]Harnstoff, Hydrochloridsalz	Behandlung des Nebennierenrindenkarzinoms
Greek	N-[2,6-δις(1-μεθυλαιθυλ)φαινυλο]-N'-[[1-[4-(διμεθυλαμινο) φαινυλο]κυκλοπεντυλ]μεθυλ]ουρία, υδροχλωρικό άλας	Θεραπεία φλοιοεπινεφριδιακού καρκινώματος

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	N-[2,6-bisz(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urea hidroklorid	Mellékvesekéreg carcinoma kezelése
Italian	N-[2,6-bis(1-metil-etil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil]urea, sale cloridrato	Trattamento del carcinoma adrenocorticale
Latvian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urīnviela, hidrohlorīda sāls	Adrenokortikālās karcinomas ārstēšana
Lithuanian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]šlapalas, hidrochlorido druska	Antinkščių žievės karcinomos gydymas
Maltese	N-[2,6-bis(1-methylethyl)phenyl]-N'-[[1-[4-(dimethylamino) phenyl]cyclopentyl]methyl]urea, hydrochloride salt	Kura ta' karċinoma adrenokortikali
Polish	Chlorowodorek N-[2,6-bis(1-metyloetylo)fenylo]-N'-[[1-[4-(dimetyloamino) fenylo]cyklopentylo]metylo]mocznika	Leczenie raka kory nadnercza
Portuguese	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil] ciclopentil] metil] ureia, sal de cloridrato	Tratamento do carcinoma adrenocortical
Romanian	Sare clorhidrat de N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil] uree	Tratamentul carcinomului corticosuprarenalian
Slovak	Chlorid N-[2,6-bis(1-metyletyl)fenyl]-N'-[[1-[4-(dimetylamino) fenyl]cyklopentyl]metyl]urey	Liečba karcinómu kôry nadobličky
Slovenian	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciklopentil]metil]urea, hidrokloridna sol	Zdravljenje karcinoma skorje nadledvične žleze
Spanish	N-[2,6-bis(1-metiletil)fenil]-N'-[[1-[4-(dimetilamino) fenil]ciclopentil]metil]urea, sal clorhidrato	Tratamiento del carcinoma adrenocortical
Swedish	N-[2,6-bis(1-metýletýl)fenýl]-N'-[[1-[4-(dímetýlamínó) fenýl]cýclópentýl]metýl]úrea, hýdróklóríð salt	Behandling av adrenokortikalt karcinom
Norwegian	N-[2,6-bis(1-metyletyl)fenyl]-N'-[[1-[4-(dimetylamino) fenyl]syklopentyl]metyl]urea,	Behandling av adrenokortikalt karsinom

Language	Active ingredient	Indication
Icelandic	N-[2,6-bis(1-metýletýl)fenýl]-N'-[[1-[4-(dímetýlamínó) fenýl]cýclópentýl]metýl]úrea, hýdróklóríð salt	Meðferð við krabbameini í nýrnahettuberki