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Public summary of opinion on orphan designation

4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazol-2-amine for the treatment of congenital adrenal hyperplasia

On 21 August 2019, orphan designation EU/3/19/2194 was granted by the European Commission to Neurocrine Therapeutics Limited, Ireland, for 4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazol-2-amine for the treatment of congenital adrenal hyperplasia.

What is congenital adrenal hyperplasia?

Congenital adrenal hyperplasia is a group of inherited conditions where patients' adrenal glands (two small glands located above each kidney) are unable to produce normal amounts of the steroid hormones cortisol and aldosterone. These hormones are important for dealing with stress and regulating salt and water in the body. In patients with the condition, these glands may produce increased amounts of male sex hormones. 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 a long-term debilitating and life-threatening condition because it can reduce the ability of the body to deal with physical stress, change the amounts of salt and water in the body, and reduce blood pressure. The condition can also cause early puberty in boys and development of masculine characteristics in girls, which can lead to growth stopping early and reduced height.

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

At the time of designation, congenital adrenal hyperplasia affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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 518,400,000 (Eurostat 2019).

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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 suggest that it improves the production of steroid 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?

The medicine is expected to work by binding to and blocking a receptor (target) on cells for a substance called CRF that is involved in abnormal hormone production of the adrenal glands. This is expected to block CRF activity and bring hormone production closer to normal, so that the patient needs lower doses of steroid medicines.

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 the treatment of congenital adrenal hyperplasia or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 July 2019, 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.

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	4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazol-2-amine	Treatment of congenital adrenal hyperplasia
Bulgarian	4-(2-хлоро-4-метокси-5-метилфенил)-N-[(1S)-2-циклопропил-1-(3-флуоро-4-метилфенил)етил]-5-метил-N-(2-пропинил)-1,3-тиазол-2-амин	Лечение на вродена надбъбречна хиперплазия
Croatian	4-(2-kloro-4-metoksi-5-metilfenil)-N-[(1S)-2-ciklopropil-1-(3-fluoro-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-amin	Liječenje kongenitalne adrenalne hiperplazije
Czech	4-(2-chlor-4-methoxy-5-methylfenyl)-N-[(1S)-2-cyklopropyl-1-(3-fluor-4-methylfenyl)ethyl]-5-methyl-N-(2-propinyl)-1,3-thiazol-2-amin	Léčba vrozené hyperplasie nadledvin
Danish	4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazol-2-amin	Behandling af medfødt binyrebarkhyperplasi
Dutch	4-(2-chloor-4-methoxy-5-methylfenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluor-4-methylfenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazool-2-amine	Behandeling van congenitale bijnierhyperplasia
Estonian	4-(2-kloro-4-metoksü-5-metüülfenüül)-N-[(1S)-2-tsüklopropüül-1-(3-fluoro-4-metüülfenüül)etüül]-5-metüül-N-(2-propünüül)-1,3-tiasool-2-amiin	Kaasasündinud neerupealise hüperplaasia ravi
Finnish	4-(2-kloro-4-metoksi-5-metyylifenyyli)-N-[(1S)-2-syklopropyyli-1-(3-fluoro-4-metyylifenyyli)etyyli]-5-metyyli-N-(2-propynyyli)-1,3-tiatsol-2-amiini	Lisämunuaisen synnynnäisen liikakasvun hoito
French	4-(2-chloro-4-méthoxy-5-méthylphényl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-méthylphényl)éthyl]-5-méthyl-N-(2-propynyl)-1,3-thiazol-2-amine	Traitmement de l'hyperplasie surrénale congénitale
German	4-(2-Chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(2-propynyl)-1,3-thiazol-2-amin	Behandlung der Kongenitalen Adrenalen Hyperplasie
Greek	4-(2-χλωρο-4-μεθοξυ-5-μεθυλφαινυλ)-N-[(1S)-2-κυκλοπροπυλ-1-(3-φθορο-4-μεθυλφαινυλ)εθυλ]-5-μεθυλ-N-(2-προπυνυλ)-1,3-θειαζολ-2-αμίνη	Θεραπεία της συγγενούς επινεφριδιακής υπερπλασίας
Hungarian	4-(2-klór-4-metoxi-5-metilfenil)-N-[(1S)-2-ciklopropil-1-(3-fluor-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-thiazol-2-amin	Congenitalis adrenalis hyperplasia kezelése
Italian	4-(2-cloro-4-metossi-5-metilfenil)-N-[(1S)-2-cyclopropil-1-(3-fluoro-4- metilfenile)etile]-5-metile-N-(2-propinile)-1,3-tiazolo-2-ammina	Trattamento dell'iperplasia surrenale congenita

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	4-(2-hlor-4-metoksi-5-metilfenil)-N-[(1S)-2-ciklopropil-1-(3-fluor-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-amīns	Iedzimtas virsnieru hiperplāzijas ārstēšana
Lithuanian	4-(2-chloro-4-metoksi-5-metilfenil)-N-[(1S)-2-ciklopropil-1-(3-fluoro-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-aminas	Įgimtos antinksčių hiperplazijos gydymas
Maltese	4-(2-kloro-4-methoksi-5-metilpfenil)-N-[(1S)-2-ċiklopropil-1-(3-fluworo-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-thiazol-2-amina	Kura ta' l-iperplasija adrenali konġenitali
Polish	4-(2-chloro-4-metoksy-5-metylofenylo)-N-[(1S)-2-cyklopropylo-1-(3-fluoro-4-metylofenylo)etylo]-5-metylo-N-(2-propynylo)-1,3-tiazolo-2-amina	Leczenie wrodzonego przerostu nadnerczy
Portuguese	4-(2-cloro-4-metoxi-5-metilfenil)-*N*-[(1*S*)-2-ciclopropil-1-(3-fluoro-4-metilfenil)etil]-5-metil-*N*-(2-propinil)-1,3-tiazol-2-amina	Tratamento da hiperplasia adrenal congenita
Romanian	4-(2-cloro-4-metoxi-5-metilfenil)-N-[(1S)-2-ciclopropil-1-(3-fluor-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-amină	Tratamentul hiperplaziei congenitale corticosuprarenale
Slovak	4-(2-chlór-4-metoxy-5-metylfenyl)-N-[(1S)-2-cyklopropyl-1-(3-fluór-4-metylfenyl)etyl]-5-metyl-N-(2-propinyl)-1,3-tiazol-2-amín	Liečba kongenitálnej nadobličkovej hyperplázie
Slovenian	4-(2-kloro-4-metoksi-5-metilfenil)-N-[(1S)-2-ciklopropil-1-(3-fluoro-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-amin	Kongenitalna adrenalna hiperplazija
Spanish	4-(2-cloro-4-metoxi-5-metilfenil)-N-[(1S)-2-ciclopropil-1-(3-fluoro-4-metilfenil)etil]-5-metil-N-(2-propinil)-1,3-tiazol-2-amina	Tratamiento de la hiperplasia suprarrenal congénita
Swedish	4-(2-klor-4-metoxy-5-metylfenyl)-N-[(1S)-2-cyklopropyl-1-(3-fluor-4-metylfenyl)etyl]-5-metyl-N-(2-propynyl)-1,3-tiazol-2-amin	Behandling av adrenogenitalt syndrom
Norwegian	4-(2-klor-4-metoksy-5-metylfenyl)-N-[(1S)-2-syklopropyl-1-(3-fluor-4-metylfenyl)etyl]-5-metyl-N-(2-propynyl)-1,3-tiazol-2-amin	Behandling av kongenitt binyrebarkhyperplasi
Icelandic	4-(2-klóró-4-metoxý-5-metýlfenýl)-N-[(1S)-2-sýklóprópýl-1-(3-flúoró-4-metýlfenýl)etýl]-5-metýl-N-própýnýl)-1,3-þíasól-2-amín	Meðfædd nýrnahettu hyperplasía