25 February 2019
EMA/818775/2018

Public summary of opinion on orphan designation

Adeno-associated viral vector expressing human 21-hydroxylase for the treatment of congenital adrenal hyperplasia

On 14 December 2018, orphan designation (EU/3/18/2108) was granted by the European Commission to Pharma Gateway AB, Sweden, for adeno-associated viral vector expressing human 21-hydroxylase 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 on the body 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 517,400,000 (Eurostat 2018).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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 laboratory data suggest that it improves production of steroid hormones without the need for corticosteroids.

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?

Most patients with congenital adrenal hyperplasia have mutations in the gene responsible to produce the enzyme 21-hydroxylase, which is one of the enzymes involved in the production of cortisol and aldosterone. Because of these mutations, patients lack 21-hydroxylase and are therefore unable to produce normal amounts of these hormones.

This medicine is made of a virus containing a normal copy of the gene for 21-hydroxylase. The virus is expected to deliver the gene into adrenal gland cells and enable them to produce the enzyme. This is expected to help relieve symptoms of the disease.

The type of virus used in this medicine ('adeno-associated virus') does not cause disease in humans.

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 congenital adrenal hyperplasia had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital adrenal hyperplasia 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 November 2018 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 the 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	Adeno-associated viral vector expressing human 21-hydroxylase	Treatment of congenital adrenal hyperplasia
Bulgarian	Адено-асоцииран вирусен вектор, експресиращ човешка 21-хидроксилаза	Лечение на вродена надбъбречна хиперплазия
Croatian	Adeno-povezani virusni vektor koji eksprimira ljudsku 21-hidroksilazu	Liječenje kongenitalne adrenalne hiperplazije
Czech	Adeno- asociovaný virální vektor exprimující humánní 21-hydroxylázu	Léčba vrozené hyperplasie nadledvin
Danish	Adeno-associeret viral vektor, der udtrykker human 21-hydroxylase	Behandling af medfødt binyrebarkhyperplasi
Dutch	Adeno-geassocieerde virale vector welke humaan 21-hydroxylase uitdrukt	Behandeling van congenitale bijnierhyperplasia
Estonian	Inimese 21-hüdroksülaasi ekspresseeriv adeno-assotsieerunud viirusvektor	Kaasasündinud neerupealise hüperplaasia ravi
Finnish	Adenoassosioitu virusvektori, joka ilmentää ihmisen 21-hydroksylaasia	Lisämunuaisen synnynnäisen liikakasvun hoito
French	Vecteur viral adéno-associé exprimant la 21-hydroxylase humaine	Traitmement de l'hyperplasie surrénale congénitale
German	Adeno-assoziierter viraler Vektor der humane 21-Hydroxylase expremiert	Behandlung der Kongenitalen Adrenalen Hyperplasie
Greek	Αδενοσχετιζόμενος ιικός φορέας που εκφράζει την ανθρώπινη 21-υδροξυλάση	Θεραπεία της συγγενούς επινεφριδιακής υπερπλασίας
Hungarian	Humán 21-hydroxylázt expresszáló adeno-asszociált virus vektor	Congenitalis adrenalis hyperplasia kezelése
Italian	Vettore virale adeno-associato che esprime la 21-idrossilasi umana	Trattamento dell'iperplasia surrenale congenita
Latvian	Adeno-asociētā vīrusa vektors, kas ekspresē cilvēka 21-hidroksilāzi	Iedzimtas virsnieru hiperplāzijas ārstēšana
Lithuanian	Adeno asocijuoto viruso vektorius, ekspresojantis 21-hidroksilazę	Įgimtos antinksčių hiperplazijos gydymas
Maltese	Vettur virali assoċjat ma' adeno li jesprimi idrossilaži-21	Kura ta' l-iperplasija adrenali konġenitali
Polish	Wirus związany z adenowirusami eksprymujący ludzką 21-hydroksylazę steroidową	Leczenie wrodzonego przerostu nadnerczy
Portuguese	Vírus adeno-associado de serotipo expressando a 21-hidroxilase humana	Tratamento da hiperplasia adrenal congenita
Romanian	Vector viral adeno-asociat ce exprimă hidroxilaza-21 umană	Tratamentul hiperplaziei congenitale corticosuprarenale
Slovak	Adeno-asociovaný vírusový vektor exprimujúci ľudskú 21-hydroxylázu	Liečba kongenitálnej nadobličkovej hyperplázie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Adeno-pridruženi virusni vector, ki eksprimira človeško 21-hidroksilazo	Kongenitalna adrenalna hiperplazija
Spanish	Vírus adeno-associado de serotipo expressando al 21-hidroxilase humana	Tratamiento de la hiperplasia suprarrenal congénita
Swedish	Adenoassocierad virusvektor som uttrycker humant 21-hydroxylas	Behandling av adrenogenitalt syndrom
Norwegian	Adenoassosiert virusvektor som uttrykker humant 21-hydroksylase	Behandling av kongenitt binyrebarkhyperplasi
Icelandic	Adenó-tengd veiruferja sem tjáir manna 21-hýdroxýlasa	Meðfædd nýrnahettu hyperplasía