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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter for the treatment of achromatopsia caused by mutations in the *CNGA3* gene

On 12 December 2016, orphan designation (EU/3/16/1795) was granted by the European Commission to Universitätsklinikum Tübingen, Germany, for adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter for the treatment of achromatopsia caused by mutations in the *CNGA3* gene.

What is achromatopsia caused by mutations in the *CNGA3* gene?

Achromatopsia is an inherited disease of the eye that leads to reduced visual acuity (how well a person can see), colour blindness, severe photophobia (eye discomfort in bright or even normal light) and nystagmus (fast involuntary eye movements). Achromatopsia affects the retina, the light-sensitive surface at the back of the eye. In patients with achromatopsia, retina cells called 'cone photoreceptors' do not work normally. These cells are needed to see in bright light and for seeing colours.

Achromatopsia is often caused by mutations (changes) in the *CNGA3* gene. It is a long-term debilitating disease because it affects how well a person can see in bright light, which may limit everyday activities.

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

At the time of designation, achromatopsia caused by mutations in the *CNGA3* gene affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating achromatopsia. Patients with the condition were given glasses with red-coloured lenses to reduce discomfort from bright light, as well as glasses to help with reading and seeing at long distance.

How is this medicine expected to work?

In this disease, a protein involved in the normal functioning of cone photoreceptors, called the CNGA3 protein, does not work properly due to defects in the gene responsible for producing it.

This medicine is made up of a virus that contains normal copies of the *CNGA3* gene. When injected into the patient's eyes, it is expected that the virus will carry the *CNGA3* gene into photoreceptor cells, so that a working CNGA3 protein can be produced. This is expected to enable cone photoreceptors to work properly, thereby improving the symptoms of the disease.

The 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, clinical trials with the medicine in patients with achromatopsia caused by mutations in the *CNGA3* gene were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for achromatopsia caused by mutations in the *CNGA3* gene 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 4 November 2016 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	Adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter	Treatment of achromatopsia caused by mutations in the *CNGA3* gene
Bulgarian	Адено-свързан вирусен вектор серотип 8, съдържащ човешкия *CNGA3* ген контролиран от промотора на арестина в зрителните колбички	Лечение на ахроматопсия, предизвикана от мутации в *CNGA3* гена
Croatian	Adeno vezani virusni vektor serotipa 8 koji sadrži ljudski *CNGA3* gen pod kontrolom promotora arestina čunjića	Liječenje akromatopsije uzrokovane mutacijama gena *CNGA3*
Czech	Adeno-asociovaný virový vektor sérotypu 8, který obsahuje lidský gen *CNGA3* pod kontrolou čípkového promotoru arestínu	Léčba achromatopsie způsobené mutacemi v genu *CNGA3*
Danish	Adeno-associeret viral vektor som indeholder det humane *CNGA3*-gen kontrolleret genom en tap arrestin promoter	Behandling af akromatopsi, forårsaget af mutationer i *CNGA3*-genet
Dutch	Adeno-geassocïeerde virale vector serotype 8 die het humane *CNGA3* gen bevat onder controle van de kegel arrestin promotor	Behandeling van door mutaties in het *CNGA3*-gen veroorzaakte achromatopsie
Estonian	Inimese *CNGA3* geeni sisaldav adenoassotsieerunud viirusvektori 8. serotüüp, mis on koonuse arrestiini promootori kontrolli all	*CNGA3* geeni mutatsioonidest põhjustatud akromatopsia ravi
Finnish	Ihmisen *CNGA3* geenin sisältävä adenoassosioitu serotyypin 8 virusvektori , joka on tappisolun arrestiini promoottorin säätelemä	*CNGA3*-geenin mutaation aiheuttaman akromatopsian hoito
French	Vecteur viral adéno-associé du sérotype 8 qui contient le gène *CNGA3* humain sous le contrôle du promoteur de l'arrestine des cônes.	Traitement de l'achromatopsie causée par des mutations du gène *CNGA3*
German	Adeno-assoziierter viraler Vektor Serotyp 8, der das humane *CNGA3* Gen unter Kontrolle des Zapfen Arrestin Promotors enthält	Behandlung von Achromatopsie infolge von Mutationen des *CNGA3*-Gens
Greek	Αδενο-σχετιζόμενος ιικός φορέας οροτύπου 8 που περιέχει το ανθρώπινο γονίδιο *CNGA3* υπό τον έλεγχο ενός υποκινητή αρρεστίνης κωνίων	Θεραπεία της αχρωματοψίας που προκαλείται από μεταλλαγές στο γονίδιο *CNGA3*
Hungarian	Adeno-asszociált virus vektor szerotípus 8, mely a humán *CNGA3* gént a csap-arrestin promoter kontrollja alatt tartalmazza	*CNGA3* gén mutációk által okozott achromatopsia kezelése
Italian	Vettore virale ricombinante adeno-associato del sierotipo 8, contenente il gene *CNGA3* umano sotto il controllo del promotore conale dell'arrestina	Trattamento della acromatopsia causata da mutazioni del gene *CNGA3*

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Adeno-asociētā vīrusa vektora 8. serotips, kas satur cilvēka *CNGA3* gēnu, kuru kontrolē vālīšu arestīna promoters	*CNGA3* gēna mutāciju izraisītas ahromatopsijas ārstēšana
Lithuanian	Su adeno virusu susietas 8 serotipo vektorius, turintis žmogaus *CNGA3* geną, kontroliuojamą kūgelių arestino promotoriaus	Achromatopsijos, sąlygotos mutacijų *CNGA3* gene, gydymas
Maltese	Vettur virali tas-serotip 8 assoċjat ma' Adeno li fih il-ġene *CNGA3* uman taħt il-kontroll tal-promotur arrestin kon	Kura tal-akromatopsija kkawżata minn mutazzjonijiet fil-ġene tas-*CNGA3*
Polish	Wektor wirusowy związany z adenowirusami (AAV) o serotypie 8, zawierający ludzki gen *CNGA3* pod kontrolą promotora arestyny komórek czopkowych	Leczenie ślepoty barw wywołanej mutacjami genu *CNGA3*
Portuguese	Vetor viral adeno-associado de serotipo 8 contendo o gene humano *CNGA3* sob o controlo de um promotor da cone arrestina	Tratamento de acromatopsia causada pelas mutações no gene *CNGA3*
Romanian	Vector viral adeno-asociat de serotip 8 ce conţine gena umană *CNGA3* sub controlul promotorului arestinei din celulele cu conuri	Tratamentul acromatopsiei produse de mutaţii ale genei *CNGA3*
Slovak	Adeno-asociovaný vírusový vektor sérotypu 8, ktorý obsahuje ľudský gén *CNGA3* pod kontrolou čapíkového promotoru arestínu	Liečba achromatopsie spôsobenej mutáciami v géne *CNGA3*
Slovenian	Adenoasocirani virusni vektor serotipa 8, ki vsebuje človeški *CNGA3* gen pod kontrolo promotorja arestina v čepnicah	Zdravljenje akromatopsije, ki jo povzročijo mutacije gena *CNGA3*
Spanish	Vector viral adenoasociado recombinante serotipo 8 que contiene el gen *CNGA3* humano bajo el control de un promotor de cone arrestin	Tratamiento de la acromatopsia causada por mutaciones en *CNGA3*
Swedish	Rekombinant adeno-associerad virusvektor som innehåller den humana *CNGA3*-genen kontrollerad genom en tapp arrestin promoter	Behandling av akromatopsi orsakad av mutationer i *CNGA3*-genen
Norwegian	Rekombinant adenoassosiert virusvektor serotype 8 som inneholder det humane *CNGA3*-genet kontrollert av en cone arrestin promoter	Behandling av akromatopsi forårsaket av mutasjoner i *CNGA3*-genet
Icelandic	Raðbrigða adenótengd veiru ferja sem inniheldur manna *CNGA3* gen undir stjórn keilu arrestin promoter	Meðferð á allitblindu af völdum stökkbreytinga í *CNCB3* geninu