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Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype 5 encoding *Staphylococcus aureus* Cas9 endonuclease and two guide RNAs complementary to two regions of intron 26 of the CEP290 gene for the treatment of Leber's congenital amaurosis

On 16 October 2017, orphan designation (EU/3/17/1928) was granted by the European Commission to Pharma Gateway AB, Sweden, for recombinant adeno-associated viral vector serotype 5 encoding *Staphylococcus aureus* Cas9 endonuclease and two guide RNAs complementary to two regions of intron 26 of the CEP290 gene (also known as EDIT-101) for the treatment of Leber's congenital amaurosis.

What is Leber's congenital amaurosis?

Leber's congenital amaurosis is an inherited disease characterised by loss of sight at birth or soon after birth. The disease is linked to a number of genetic mutations (changes), which affect the normal development of the light-sensitive cells in the eye.

Leber's congenital amaurosis is a long-term debilitating disease due to the progressive loss of sight.

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

At the time of designation, Leber's congenital amaurosis 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).

What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating Leber's congenital amaurosis. Patients with the condition usually received regular medical follow up, vision aids and genetic counselling on the risks of passing the condition on to their children.

*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).

How is this medicine expected to work?

Mutations (changes) in the *CEP290* gene are among the known mutations that cause Leber's congenital amaurosis. As a result of these mutations, patients do not produce enough of a protein called CEP290 that works properly. CEP290 has an important role in the development of the light-sensitive cells in the eye.

The medicine is made of a virus that, when injected into the eye, delivers genetic material into light-sensitive cells in the eye. This genetic material is expected to remove or modify the part of the *CEP290* gene that contains the mutation. This is expected to lead to the production of a functional CEP290 protein, thus allowing the light sensitive cells in the eye to develop properly.

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?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with Leber's congenital amaurosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Leber's congenital amaurosis 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 7 September 2017 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, 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant adeno-associated viral vector serotype 5 encoding <i>Staphylococcus aureus</i> Cas9 endonuclease and two guide RNAs complementary to two regions of intron 26 of the <i>CEP290</i> gene	Treatment of Leber's congenital amaurosis
Bulgarian	Рекombинантен адено-асоцииран вирусен вектор, серотип 5, кодиращ Cas9 ендонуклеаза от <i>Staphylococcus aureus</i> и 2 водещи РНК, комплементарни на 2 региона на интрон 26 от <i>CEP290</i> гена	Лечение на вродена амавроза на Лебер
Croatian	Rekombinantni adeno-povezani virusni vektor serotipa 5 koji kodira <i>Staphylococcus aureus</i> Cas9 endonukleazu i dva RNA vodiča komplementarna s dvije regije introna 26 gena <i>CEP290</i>	Liječenje Leberove kongenitalne amauroze
Czech	Rekombinantní adeno-asociovaný virový vektor serotypu 5 kódující endonukleázu Cas9 <i>Staphylococcus aureus</i> a dvě řídící RNA (gRNA) komplementární ke dvěma regionům intronu 26 genu <i>CEP290</i>	Léčba Leberovy vrozené slepoty
Danish	Rekombinant adenoassocieret viral vektor serotype 5, der koder for <i>Staphylococcus aureus</i> Cas9 endonuclease og to styrende RNA'er komplementære til to regioner af intron 26 af <i>CEP290</i> genet.	Behandling af Lebers kongenitte amaurose
Dutch	Recombinant adeno-geassocieerde viral vector serotype 5 welke codeert voor <i>Staphylococcus aureus</i> Cas9 endonuclease and twee begeleidende RNAs complementair aan twee regionen van intron 26 uit het <i>CEP290</i> gen	Behandeling van amaurosis congenita van Leber
Estonian	Rekombinantne adonoviirusega assotseerunud viirusvektor 5, mis kodeerib <i>Staphylococcus aureus</i> Cas9 endonukleaasi ja <i>CEP290</i> geeni 26. introni kahe piirkonna 2 juhte RNA-d	Leberi tüüpi kaasasündinud amauroosi ravi
Finnish	Rekombinantti serotyypin 5 adenoassosioitu virusvektori, joka koodaa <i>Staphylococcus aureus</i> Cas9:n endonukleasia ja kahta opas-RNA:ta täydentävänä <i>CEP290</i> geenin kahdelle introni 26:n alueelle	Leberin synnynnäisen amauroosin (sokeus) hoito
French	Vecteur adénoviral recombinant du sérotype 5 contenant une endonuclease <i>Staphylococcus aureus</i> Cas9 et deux guides ARNs complémentaires des deux régions de l'intron 26 du gene <i>CEP290</i>	Traitement de l'amaurose congénitale de Leber

¹ At the time of designation

Language	Active ingredient	Indication
German	Rekombinanter adeno-assoziiertes viraler Vektor vom Serotyp 5 der für die <i>Staphylococcus aureus</i> Cas9 Endonuklease und für zwei Guide-RNAs, die komplementär zu zwei Regionen des Introns 26 des <i>CEP290</i> Gens sind, kodiert	Behandlung der Leberschen Kongenitalen Amaurose
Greek	Ανασυνδυασμένος αδενο-σχετιζόμενος ιϊκός φορέας οροτύπου 5 που κωδικοποιεί την ενδονουκλεάση Cas9 του χρυσίζοντος σταφυλοκόκκου και δύο οδηγά μόρια RNA συμπληρωματικά δύο περιοχών του εσωνίου 26 του γονιδίου <i>CEP290</i>	Θεραπεία τής συγγενούς αμαύρωσης του Leber
Hungarian	<i>Staphylococcus aureus</i> Cas9 endonukleáz és a <i>CEP290</i> gén 26-os intronjának két régióját komplementáló újmutató RNS-t kódoló 5-ös szerotípusú rekombináns adeno-asszociált virális vektor	Leber-féle hereditaer opticus atrophia kezelése
Italian	Vettore adenovirale ricombinante di serotipo 5 contenente l'endonucleasi <i>Staphylococcus aureus</i> Cas9 et due guide RNA complementari a due regioni dell'introne 26 del gene <i>CEP290</i>	Trattamento dell'amaurosi congenita di Leber
Latvian	Rekombinants adeno-saistītā vīrusa vektora 5. serotips, kas kodē <i>Staphylococcus aureus</i> Cas9 endonukleāzi un divas vadošās RNS (gRNS), kas papildina divus <i>CEP290</i> gēna 26. introna reģionus	Iedzimta Lēbera akluma ārstēšana
Lithuanian	Rekombinantinis adeno asocijuotas viruso vektoriaus 5 serotipas, koduojantis <i>Staphylococcus aureus</i> Cas9 endonuklezę ir dvi lydinčias RNR, komplementarias dviems <i>CEP290</i> geno 26 introno sritims	Įgimtos Lėberio amaurozės gydymas
Maltese	Vettur virali serotip 5 adeno-assoċjat rikombinant li jikkodifika <i>Staphylococcus aureus</i> Cas9 endonukleazi u żewġ RNAs ta' gwida kumplimentari għal żewġ reġjuni ta' intron 26 tal-gene <i>CEP290</i>	Kura ta' l-amawrozi kongenitali ta' Leber
Polish	Rekombinowany związany z adenowirusami wektor wirusowy serotypu 5 kodujący endonukleazę <i>Staphylococcus aureus</i> Cas9 oraz dwa przewodnie łańcuchy RNA komplementarne do dwóch regionów intronu 26 genu <i>CEP290</i>	Leczenie wrodzonej ślepoty Lebera
Portuguese	Vírus viral adeno-associado recombinante de serotipo 5 que codifica a endonuclease Cas9 de <i>Staphylococcus aureus</i> e dois RNAs guia complementares a duas regiões do intrão 26 do gene <i>CEP290</i>	Tratamento do Amaurose Congénita de Leber
Romanian	Vector viral recombinant adeno-asociat de serotip 5 ce codifică endonucleaza Cas9 a <i>Staphylococcus aureus</i> și două secvențe ARN _s ghid complementare pentru două regiuni ale intronului 26 al genei <i>CEP290</i>	Tratamentul amaurozei congenitale Leber

Language	Active ingredient	Indication
Slovak	Rekombinantný adeno-asociovaný virálny vektor sérotypu 5 kódujúci Cas9 endonukleázu <i>Staphylococcus aureus</i> a dve navádzacie RNA komplementárne k dvom regiónom intrónu 26 <i>CEP290</i> génu	Liečba Leberovej vrodenej amaurózy
Slovenian	Rekombinantni, adenovirusom pridružen virusni vektor serotipa 5, kodiran za endonukleazo <i>Staphylococcus aureus</i> Cas9 and dva vodiča RNK, komplementarna dvema mestoma introna A 26 gena <i>CEP290</i>	Zdravljenje Leberjeve vrojene amavroze
Spanish	Virus viral adeno-asociado recombinante de serotipo 5 que codifica la endonuclease Cas9 de <i>Staphylococcus aureus</i> y dos RNAs guía complementares a las dos regiones del intron 26 del gene <i>CEP290</i>	Tratamiento de la amaurosis congénita de Leber
Swedish	Rekombinant adenoassocierad viral vektor serotype 5, som kodar för <i>Staphylococcus aureus</i> Cas9 endonucleas och två guide-RNA associerade till två regioner på intron 26 af <i>CEP290</i> genen.	Behandling av Lebers kongenitala amauros
Norwegian	Rekombinant adenoassosiert virusvektor serotype 5 som koder for <i>Staphylococcus aureus</i> Cas9 endonuklease og to guide-RNA komplementære til to regioner av intron 26 i genet for <i>CEP290</i>	Behandling av Lebers kongenitale amaurose
Icelandic	Raðbrigða adenótengd veiruvektor sermisgerð 5 sem kóðar fyrir <i>Staphylococcus aureus</i> Cas9 endónúkleasa og to guide-RNA komplementare gegn intron 26 í <i>CEP290</i> geni	Meðferð á Leber meðfæddri blindu