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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector containing the human *NADH dehydrogenase 4* gene for the treatment of Leber's hereditary optic neuropathy

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Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Commc```ittee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 13 May 2011, orphan designation (EU/3/11/860) was granted by the European Commission to Institut de la Vision, France, for adeno-associated viral vector containing the human NADH dehydrogenase 4 gene for treatment of Leber's hereditary optic neuropathy.

The sponsorship was transferred to Gensight-Biologics, France, in September 2013.

What is Leber's hereditary optic neuropathy?

Leber's hereditary optic neuropathy is a hereditary disease of the optic nerve, the nerve at the back of the eye that transmits signals to the brain. The disease is due to mutations in the mitochondrial genes which render the mitochondria, the energy-producing components within cells, unable to work properly. Patients inherit the mutation from their mother. While all children of an affected mother carry the mutation, not all are affected by the disease. Those who are affected (about 80% of the sons and half of the daughters) rapidly lose their sight over a period of few months by their mid-twenties. The reason why patients start to lose their sight is unclear, but environmental and lifestyle factors such as smoking or alcohol consumption may play a role.

Leber's hereditary optic neuropathy is a long-term debilitating disease because of the visual loss and development of blindness.

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

At the time of designation, Leber's hereditary optic neuropathy affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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, there were no satisfactory methods authorised in the EU for the treatment of Leber's hereditary optic neuropathy. Patients carrying the genetic mutation were advised to avoid lifestyle factors known to be involved in triggering the onset of blindness, such as smoking and alcohol consumption.

How is this medicine expected to work?

Adeno-associated viral vector containing the human *NADH dehydrogenase 4* gene is a medicine that works by delivering genes into the body. It is made up of a virus that contains the gene for an enzyme called 'NADH dehydrogenase 4'. Patients who carry the genetic mutation that cause Leber's hereditary optic neuropathy have mitochondria that cannot function normally as they are not able to produce this enzyme. The medicine is expected to be injected into the optic nerve, where the virus will deliver the gene so that the enzyme can be produced and the mitochondrial function can be improved. This is expected to prevent or slow down the loss of vision.

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 adeno-associated viral vector containing the human *NADH dehydrogenase 4* gene 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 Leber's hereditary optic neuropathy had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Leber's hereditary optic neuropathy 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 9 February 2010 recommending the granting of this designation.

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[*]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.
At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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:
Gensight-Biologics
89 rue du Faubourg St Antoine
75011 Paris
France
Tel.: +33 6 65 03 86 01
http://www.gensight-biologics.com/contacts/send

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 containing the human *NADH dehydrogenase 4* gene	Treatment of Leber's hereditary optic neuropathy
Bulgarian	Аденосвързан вирусен вектор, съдържащ човешки ензим *NADH 4* ген	Лечение на наследствена оптична невропатия на Leber
Croatian	Adeno-povezani virusni vektor koji sadrži ljudski gen za *NADH dehidrogenazu 4*	Liječenje Leberove nasljedne optičke neuropatije
Czech	Adeno-asociovaný virový vektor obsahující lidský gen *NADH-dehydrogenázy 4*	Léčba Leberovy hereditární optické neuropatie
Danish	Adeno-associeret viral vektor der indeholder det humane *NADH dehydrogenase 4* gen	Behandling af Lebers hereditære opticusneuropati
Dutch	Adenogeassocieerde virale vector, welke het humaan *NADH dehydrogenase 4* gen bevat	Behandeling van Leber hereditaire optische neuropathie
Estonian	Adenoviirusega seotud viirusevektor, mis sisaldab inimese *NADH dehüdrogenaas 4* geeni	Leberi päriliku optilise neuropaatia ravi
Finnish	Adeno-assosioitu virusvektori, joka sisältää ihmisen *NADH dehydrogenaasi 4* geenin	Leberin atrofian hoito
French	Vecteur viral adéno-associé contenant le gène humain de la *NADH deshydrogénase 4*	Traitement de la neuropathie optique héréditaire de Leber
German	Adeno-assoziierter viraler Vektor mit humanem NADH-Dehydrogenase-4-Gen	Behandlung der Leberschen hereditären Optikusneuropathie
Greek	Ιϊκός φορέας σχετιζόμενος με αδενοϊό που περιέχει το ανθρώπινο γονίδιο NADH αφυδραγονάση 4	Θεραπεία κληρονομικής οπτικής νευροπάθειας του Leber
Hungarian	Az emberi NADH dehidrogenáz 4 gént tartalmazó adeno-asszociált vírus vector	Leber-féle hereditaer opticus neuropathia kezelése
Italian	Vettore virale adeno-associato contenente il gene della NADH deidrogenasi 4 umana	Trattamento della neuropatia ottica ereditaria di Leber
Latvian	Cilvēka gēnu NADH 4 satušs adenosaistīts vīrusu vektors	Lēbera hereditārās optiskās neiropātijas ārstēšana
Lithuanian	Adeno-asocijuoto viruso vektorius, pernešantis žmogaus NADH dehidrogenazės 4 geną	Lėberio paveldimosios optinės neuropatijos gydymas
Maltese	Vettur imnissel mill-adenovirus li fih il-ġene NADH dehydrogenase 4 uman	Kura tan-newropatija ottika ereditarja ta' Leber
Polish	Wektor sprzężony z adenowiresum zawierający ludzki gen dehydrogenazy 4 NADPH	Leczenie dziedzicznej neuropatii Lebera nerwu wzrokowego
Portuguese	Vector Viral Adeno-Associado contendo o gene humano NADH Desidrogenase 4	Tratamento de neuropatia óptica hereditária de Leber
Romanian	Vector viral adeno-asociat care conţine gena umană pentru NADH 4 dehidrogenază	Tratamentul neuropatiei optice ereditare Leber
Slovak	Adeno-asociovaný vírusový vektor obsahujúci ľudský gén NADH-dehydrogenázy 4	Liečba Leberovej dedičnej neuropatie optického nervu

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Slovenian	Adenovirusom pridruženi virusni vektor, ki vsebuje gen za človeško NADH dehidrogenazo 4	Zdravljenje Leberjeve hereditarne optične nevropatije
Spanish	Vector viral adenoasociado que contiene el gen humano de la *NADH deshidrogenasa 4*	Tratamiento de la neuropatía óptica hereditaria de Leber
Swedish	Adeno-associerad virusvektor som innehåller den humana NADH dehydrogenas 4 genen	Behandling av Lebers hereditära optikusneuropati
Norwegian	Adenoassosiert virusvektor som inneholder humant NADH dehydrogenase 4 gen	Behandling av Lebers hereditære optikusneuropati
Icelandic	Adeno-tengd veiruferja sem inniheldur manna NADH-dehýdrógenasa 4 gen	Meðferð við arfgengum Lebers sjóntaugarkvilla