13 December 2016
EMA/685910/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein for the treatment of aromatic L-amino acid decarboxylase deficiency

On 18 November 2016, orphan designation (EU/3/16/1786) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein (also known as AGIL-AADC) for the treatment of aromatic L-amino acid decarboxylase deficiency.

What is aromatic L-amino acid decarboxylase deficiency?

Aromatic L-amino acid decarboxylase deficiency is an inherited condition affecting the nervous system. It is caused by lack of the enzyme aromatic L-amino acid decarboxylase (AADC), which is needed to produce certain substances vital for the normal function of the brain and nerves, including dopamine, and serotonin. Symptoms appear in the first year of life and include rigidity or muscle floppiness, spasms and abnormal movements, swallowing difficulties, abnormal eyeball movements, poor sleep, developmental delay and behavioural problems.

Aromatic L-amino acid decarboxylase deficiency is a long-term debilitating and life-threatening condition because it can lead to multiple organ failure.

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

At the time of designation, aromatic L-amino acid decarboxylase deficiency affected less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 500 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 method was authorised in the EU for the treatment of aromatic L-amino acid decarboxylase deficiency. Patients were mainly offered supportive treatment to manage symptoms.

How is this medicine expected to work?

Aromatic L-amino acid decarboxylase deficiency is caused by mutations (changes) in the gene that produces the AADC enzyme. The medicine consists of a virus that contains a functional version of the AADC gene. When given to the patient, it is expected that the virus will carry the AADC gene into nerve cells, enabling them to produce the missing enzyme. This in turn is expected to enable the cells to produce the substances they need to function properly (such as dopamine and serotonin), thus improving symptoms of the condition.

The virus used in this medicine (adeno-associated viral vector) 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 aromatic L-amino acid decarboxylase deficiency were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for aromatic L-amino acid decarboxylase deficiency. Orphan designation of the medicine had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 October 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	Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein	Treatment of aromatic L-amino acid decarboxylase deficiency
Bulgarian	Рекомбинантен адено-свързан вирусен вектор, серотип 2, носещ гена на човешката ароматна L-аминокиселинна декарбоксилаза	Лечение на дефицит на ароматна L-аминокиселинна декарбоксилаза
Croatian	Rekombinantni adeno-vezani virusni vektor serotipa 2 koji nosi gen za protein ljudske aromatske L-aminokiselinske dekarboksilaze	Liječenje nedostatka aromatične L-amino kiselinske dekarboksilaze
Czech	Rekombinantní adeno- asociovaný virální vector serotype 2 nesoucí gen pro humánní dekarboxylovaný protein aromatické L-aminokyselinu	Léčba deficit dekarboxylázy aromatické L- aminokyseliny
Danish	Rekombinant adeno-associeret viral vektor serotype 2 indeholdende genet for det humane aromatisk L-aminosyre decarboxylase protein	Behandling af aromatisk L-aminosyre decarboxylase mangel
Dutch	Recombinant adeno-geassocieerde virale vector serotype 2 die het gen voor humaan aromatisch L-aminozuur decarboxylase-eiwit draagt	Behandeling van aromatisch L-aminozuurdecarboxylase deficiëntie
Estonian	Inimese aromaatse aminohappe dekarboksülaasi geeni sisaldav rekombinantne adenoassotsieerunud viirusvektori 2. serotüüp	Aromaatse L-aminohappe dekarboksülaasi puudulikkuse ravi
Finnish	Rekombinantti adenoassosioitu virusvektori, serotyyppiä 2, sisältäen ihmisen aromaattisen L-aminohappo dekarboksylaatio proteiinin	Aromaattisen L-aminohappo dekarboksylaasipuutoksen hoito
French	Vecteur viral adéno-associé recombinant de sérotype 2 contenant le gène de la protéine humaine décarboxylase d'acide L-aminé aromatique	Traitement du déficit en décarboxylase d'acide L-aminé aromatique
German	Rekombinanter adeno-assoziierter viraler Vektor vom Serotyp 2, der das Gen für das humane aromatische L-Aminosäure Decarboxylase Protein enthält	Behandlung des Aromatische-L-Aminosäuredecarboxylase-Mangels
Greek	Ανασυνδυασμένος αδενο-σχετιζόμενος ιικός φορέας οροτύπου 2 που περιέχει το γονίδιο για την ανθρώπινη πρωτεΐνη της αποκαρβοξυλάσης των αρωματικών L-αμινοξέων	Θεραπεία της ανεπάρκειας της αποκαρβοξυλάσης των αρωματικών L-αμινοξέων
Hungarian	Humán aromás L-aminosav dekarboxiláz fehérje génjét hordozó 2-es szerotípusú rekombináns humán adeno-asszociált virus vektor	Aromás L-aminosav dekarboxiláz elégtelenség kezelése
Italian	Vettore ricombinante adeno-associato di serotipo virale 2 contenente il gene per la proteina decarbossilasi degli L-amino acidi aromatici	Trattamento del deficit di decarbossilasi degli L-aminoacidi aromatici

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Rekombinants adeno-asociētā vīrusa vektora 2. serotips, kas pārnēsā cilvēka aromātisko L-aminoskābju dekarboksilāzes proteīna gēnu	Aromātisko L-aminoskābju dekarboksilāzes nepietiekamības ārstēšana
Lithuanian	Rekombinantinis adeno-asocijuoto viruso vektoriaus serotipas 2, pernešantis žmogaus aromatinių L aminorūgščių dekarboksilazės baltymo geną	Aromatinių L aminorūgščių dekarboksilazės stokos gydymas
Maltese	Vettur virali serotip 2 rikombinanti assoċjat ma' adeno li jġorr il-ġene għall-proteina umana L-amino aċidu dekarbossilaži aromatika	Il-kura ta' defiċjenza L-amino aċidu dekarbossilaži aromatika
Polish	Rekombinowany wektor wirusowy związany z adenowirusami serotypu 2 zawierający gen ludzkiego białka dekarboksylazy aromatycznych L-aminokwasów	Leczenie niedoboru dekarboksylazy aromatycznych L-aminokwasów
Portuguese	Vetor viral recombinante adeno-associado de serotipo 2 com o gene humano para a proteína da descaboxilase dos L-aminoácidos aromáticos	Tratamento da deficiência da descarboxilase dos L-aminoácidos aromáticos.
Romanian	Vector viral recombinant adeno-asociat de serotip 2 ce conţine gena umană pentru proteina decarboxilază aromatică a L-aminoacizilor	Treatmentul deficitului de decarboxilază aromatică a L-aminoacizilor
Slovak	Rekombinantný adeno-asociovaný virálny vektor sérotypu 2 nesúci gén pre ľudský proteín dekarboxylázu L-aminokyseliny	Liečba deficiencie dekarboxylázy aromatickej L-aminokyseliny
Slovenian	Rekombinantni adenovirusni vector serotipa 2, ki prenaša gen človeške aromatične L-aminokislinske dekarboksilaze proteinov	Zdravljenje pomanjkanja aromatične L-aminokislinske dekarboksilaze
Spanish	Vector viral adenoasociado recombinante de serotipo 2 que continene el gen humano de la L-Aminoácido aromático descarboxilasa.	Tratamiento de la deficiencia de L-Aminoácido aromático descarboxilasa.
Swedish	Rekombinant adenoassocierad virusvektor av serotyp 2 innehållande den humana genen för aromatisk L-aminosyra-decarboxylasprotein	Behandling av aromatisk L-aminosyra-decarboxylasbrist
Norwegian	Rekombinant adenoassosiert viral vektor serotype 2 som inneholder genet for humant aromatisk L-aminosyre dekarboksylaseprotein	Behandling av aromatisk L-aminosyre dekarboksylase mangel
Icelandic	Raðbrigða adenó-tengd veiru ferja af sermisgerð 2 sem inniheldur gen fyrir manna aromatic L-amínósýru dekarboxýlasa protein	Meðferð við aromatic L-amínó sýru dekarboxýlasaskorti