27 May 2016
EMA/COMP/235552/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype 9 carrying the gene for the human E6-AP ubiquitin protein ligase for the treatment of Angelman syndrome

On 28 April 2016, orphan designation (EU/3/16/1651) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for recombinant adeno-associated viral vector serotype 9 carrying the gene for the human E6-AP ubiquitin protein ligase for the treatment of Angelman syndrome.

What is Angelman syndrome?

Angelman syndrome is an inherited disorder that mainly affects the brain. It is caused by an abnormality in the gene needed to make an enzyme called E6-AP ubiquitin ligase, which is essential for normal development of the brain. Children with this condition often have delayed development, intellectual disability, severe speech impairment, problems with movement and balance, recurrent seizures (fits) and sociable behaviour with frequent smiling.

Angelman syndrome is a long-term debilitating condition due to the developmental delay, problems with movement and seizures.

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

At the time of designation, Angelman syndrome affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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, no medicines were authorised in the EU for the treatment of Angelman syndrome. Available treatments were aimed at treating some of the symptoms of the disease such as medicines for epilepsy and behavioural therapy.

[*]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).

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

How is this medicine expected to work?

The medicine is made of a virus that has been modified to contain a working copy of the gene for E6-AP ubiquitin ligase. After being given once to the patient as an injection into the space around the spine, the virus is expected to carry the gene into the brain cells, enabling them to produce the missing protein for a long period. This is expected to improve the symptoms of the disorder.

The 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, no clinical trials with the medicine in patients with Angelman syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Angelman syndrome. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 March 2016 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant adeno-associated viral vector serotype 9 carrying the gene for the human E6-AP ubiquitin protein ligase	Treatment of Angelman syndrome
Bulgarian	Рекомбинантен адено-свързан вирусен вектор, серотип 9 носещ гена на човешката E6-AP убиквитин-протеин лигаза	Лечение на синдрома на Ангелман
Croatian	Rekombinanti adeno-povezani virusni vektor serotipa 9 koji nosi gen za ljudsku E6-AP ubikvitin protein ligazu	Liječenje Angelmanovog sindroma
Czech	Rekombinantní adeno- asociovaný virový vektor serotypu 9 nesoucí gen pro lidský E6-AP ubiquitinproteinové ligázy	Léčba Angelmanova syndromu
Danish	Rekombinant adeno-associeret viral vektor serotype 9, som bærer det humane EG-AP ubiquitin protein ligase gen	Behandling af Angelman syndrom
Dutch	Recombinant adeno-geassociëerde virale vector serotype 9 welke het gen voor het humane E6-AP ubiquitin proteïne ligase bevat	Behandeling van het syndroom van Angelman
Estonian	Inimese *E6-AP ubiquitin protein ligase* geeni sisaldav rekombinantne adenoviirusega seotud viirusvektori serotüüp 9	Angelmani sündroomi ravi
Finnish	Rekombinantti adeno-pohjainen serotyypin 9 virusvektori, jossa on mukana geeni ihmisen E6-AP ubikitiini–proteini ligaasille	Angelmanin oireyhtymän hoito
French	Vecteur viral recombinant adéno-associé de sérotype 9 portant le gène de la protéine ubiquitine ligase humaine E6-AP	Traitement du syndrome d'Angelman
German	Rekombinanter adeno-assoziierter viraler Vektor vom Serotyp 9, der das Gen für die humane E6-AP Ubiquitin Protein Ligase enthält	Behandlung des Angelman Syndroms
Greek	Ανασυνδυασμένος αδενο-σχετιζόμενος ιϊκός φορέας οροτύπου 9 που φέρει το γονίδιο για τη ανθρώπινη πρωτεϊνική λιγάση ουμπικιτίνης E6-AP	Θεραπεία του συνδρόμου Angelman
Hungarian	Humán E6-AP ubikvitin protein ligáz génjét hordozó rekombináns adeno-asszociált 9-es szerotípusú virus vektor	Angelman szindróma kezelése
Italian	Vettore virale recombinate adeno-associato di serotipo 9 che trasporta il gene della proteina ubiquitina ligase umana	Trattamento della syndrome di Angelman
Latvian	Rekombinants adeno-asociētā vīrusa vektora 9. seroptips, kas satur cilvēka E6-AP ubikvitīna proteīna ligāzes gēnu	Angelmana sindroma ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Rekombinantinis adenoasocijuoto viruso vektoriaus 9 serotipas, pernešantis žmogaus E6-AP ubikvitino baltymo ligazės geną	*Angelman* sindromo gydymas
Maltese	Vettur virali rikombinanti adeno-assoċjat tas-serotip 9 li jġorr il-ġene għal E6-AP *ubiquitin protein ligase* uman	Kura tas-sindrome ta' Angelman
Polish	Rekombinowany związany z adenowirusami wirusowy wektor serotypu 9 zawierający gen ludzkiej ligazy ubikwityna-białko E6-AP	Leczenie zespołu Angelmana
Portuguese	Vetor viral recombinante adeno-associado do serotipo 9 contendo o gene da proteína ubiquitina ligase E6-AP humana	Tratamento da síndrome de Angelman
Romanian	Vector viral adeno-asociat recombinant de serotip 9, ce poartă gena E6-AP ubicuitin protein ligazei umane	Tratamentul sindromului Angelman
Slovak	Rekombinantný adeno-asociovaný vírový vektor serotypu 9 nesúci gén pre ľudskú E6-AP proteínovú ubikvitín ligázu	Liečba Angelmanovho syndrómu
Slovenian	Rekombinantni adenovirusom pridruženi virusni vector serotipa 9, ki nosi gen za humano E6-AP ligazo proteina ibikvitin	Zdravljenje Angelmanovega sindroma
Spanish	Vector virico adenoasociado recombinante serotipo 9 que contiene el gene humano de la proteína ligasa de ubiquitina	Tratamiento del sindrome de Angelman
Swedish	Rekombinant adenoassocierad viral vector serotyp 9 innehållande den humana genen för E6-AP ubiquitin protein ligas	Behandling av Angelmans syndrom
Norwegian	Rekombinant adeno-assosiert viral vektor serotype 9 innehållende det humane genet for E6-AP ubiquitin protein ligase	Behandling av Angelmans syndrom
Icelandic	Raðbrigða adenó-tengd veiruferja sermisgerð 9 sem ber genið fyrir manna E6-AP úbiqúitín protein lígasa	Eðferð við Angelman heilkenni