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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 9 containing the human CLN1 gene for the treatment of neuronal ceroid lipofuscinosis

On 25 May 2018, orphan designation (EU/3/18/2016) was granted by the European Commission to Abeona Therapeutics Europe SL, Spain, for adeno-associated viral vector serotype 9 containing the human CLN1 gene for the treatment of neuronal ceroid lipofuscinosis.

What is neuronal ceroid lipofuscinosis?

Neuronal ceroid lipofuscinosis is a group of inherited diseases where deposits known as lipofuscins made of fats and proteins build up in the brain and other parts of the body, such as the eye, causing damage. Symptoms of the disease include delayed speech, inability to coordinate muscle movements, fits, loss of vision and mental disability.

Neuronal ceroid lipofuscinosis is a debilitating and life-threatening condition that leads to death by early adulthood.

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

At the time of designation, neuronal ceroid lipofuscinosis affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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, the medicine Brineura was authorised in the EU for the treatment of neuronal ceroid lipofuscinosis type 2. Brineura replaces the TPP1 enzyme (one of several enzymes whose absence can lead to lipofuscin build-up) which is missing in this form of the disease. The disease was also managed by treating its symptoms.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with neuronal ceroid lipofuscinosis because laboratory data show that it may

[*]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 517,400,000 (Eurostat 2018).

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improve survival and movement skills of patients with neuronal ceroid lipofuscinosis type 1, for whom no treatment exists. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

This medicine is expected to be used in patients with neuronal ceroid lipofuscinosis type 1. These patients have mutations (changes) in the *CLN1* gene that is responsible for the production of an enzyme called PPT1 needed for proper breakdown of proteins in the body. As a result, the PPT1 enzyme does not work properly, leading to build-up of lipofuscins. Because a different enzyme is involved, patients with type 1 disease cannot be treated with Brineura.

This medicine is made of a virus that contains normal copies of the *CLN1* gene. When injected into the patient, it is expected that the virus will be carried into the nerve cells enabling them to start producing a working PPT1 enzyme. This is expected to relieve the symptoms of the disease.

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 this medicine 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 neuronal ceroid lipofuscinosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for neuronal ceroid lipofuscinosis. 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 19 April 2018 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 9 containing the human *CLN1* gene	Treatment of neuronal ceroid lipofuscinosis
Bulgarian	Адено-асоцииран вирусен вектор серотип 9, съдържащ човешки *CLN1* ген	Лечение на липофусциноза на невроните
Croatian	Adeno-povezani virusni vektor serotipa 9 koji sadrži humani gen *CLN1*	Liječenje neuronske ceroidne lipofuscinoze
Czech	Adeno-asociovaný virový vektorový sérotyp 9 obsahující lidský gen *CLN1*	Léčba neuronálního ceroidu lipofuscinózy
Danish	Adeno-associeret viral vektor serotype 9 indeholdendedet humane *CLN1*-gen	Behandling af neuronal ceroid lipofuscinosis
Dutch	Adeno-geassocieerd viraal vector serotype 9 dat het menselijke *CLN1*-gen bevat	Behandeling van neuronale ceroïdlipofuscinose
Estonian	Inimese *CLN1* geeni sisaldav adeno-assotsieerunud viirusvektori 9. serotüüp	Neuronaalse tseroidse lipofustsinoosi ravi
Finnish	Adeno-assosioitu virusvektori serotyyppi 9, joka sisältää ihmisen *CLN1*-geenin	Neuronaalisen seroidilipofuskinoosin hoito
French	Vecteur viral adéno-associé sérotype 9 contenant le gène *CLN1* humain	Traitement des céroïdes-lipofuscinoses neuronales
German	Adeno-assoziierter viraler Vektor Serotyp 9, der das das humane *CLN1*-Gen enthält	Behandlung von neuronaler Ceroid-Lipofuszinose
Greek	Αδενο-σχετιζόμενος ιικός φορέας οροτύπου 9 που περιέχει το ανθρώπινο γονίδιο *CLN1*	Θεραπεία της νευρωνικής κηροειδούς λιποφουσκίνωσης
Hungarian	Humán *CLN1* gént tartalmazó 9-es adeno-társított vírusvektor	Neuronalis ceroid lipofuscinosis kezelése
Italian	Sierotipo 9 del vettore virale adeno-associato contenente il gene *CLN1* umano	Trattamento della ceroidolipofuscinosi neuronale giovanile
Latvian	Adeno saistītā vīrusa vektora 9. serotips, kas satur cilvēka *CLN1* gēnu	Neironu ceroīdās lipofuscinozes ārstēšana
Lithuanian	Adenoasocijuotas viruso vektoriaus 9 serotipas, koduojantis žmogaus *CLN1* geną	Neuronų ceroidinės lipofuscinozės gydymas
Maltese	Serotip 9 ta' vettur virali assoċjat mal-adeno li fih il-ġene umana *CLN1*	Kura ta' lipofuscinoži ċerojde Newronali
Polish	Związany z adenozą Wektor wirusowy serotypu 9 zawierający ludzki gen *CLN1*	Leczenie ceroidolipofuscynozy neuronalnej
Portuguese	Vetor viral adeno-associado de serotipo 9 que contem o gene *CLN1* humano	Tratamento da Lipofuscinose Ceroide neuronial
Romanian	Vector viral adeno-asociatde serotip 9 al care conține gena *CLN1* umană	Tratamentul lipofuscinozei ceroide neuronale
Slovak	Adeno-asociovaný vírusový vektorový sérotypu 9 obsahujúci ľudský gén *CLN1*	Liečba neurónovej ceroidnej lipofuscinózy

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Adeno-pridruženi virusni vektor serotipa 9, ki vsebuje človeški *CLN1* gen	Zdravljenje nevronske ceroidne lipofuscinoze
Spanish	Vector viral serológico asociado al serotipo 9 que contiene el gen *CLN1* humano	Tratamiento de ceroidolipofuscinosis neuronal
Swedish	Adeno-associerad viral vektor serotyp 9 innehållande den humana *CLN1*-genen	För behandling av neuronal ceroidlipofuscinos
Norwegian	Adenoassosiert viral vektor serotype 9 som inneholder det humane *CLN1*-genet	Behandling av nevronal ceroid lipofuscinose
Icelandic	Adenó tengd veiruferja af sermisgerð 9 sem kóðar fyrir manna *CLN1* genið	Meðferð á tauga ceróíð lípófuscinósis