6 May 2019
EMADOC-628903358-641

# Public summary of opinion on orphan designation

## Adeno-associated viral vector serotype rh10 containing the human cholesterol 24-hydroxylase gene for the treatment of Huntington's disease

On 1 April 2019, orphan designation (EU/3/19/2149) was granted by the European Commission to Brainvectis, France, for adeno-associated viral vector serotype rh10 containing the human cholesterol 24-hydroxylase gene for the treatment of Huntington's disease.

### What is Huntington's disease?

Huntington's disease is a hereditary disease that causes brain cells to die. This leads to symptoms such as involuntary jerky movements, behavioural problems and dementia (loss of intellectual function). The disease is usually first noticed between 35 and 45 years of age, and gets worse over time.

Huntington's disease is caused by defects in the gene responsible for the production of a protein called huntingtin. The gene abnormalities result in an abnormal form of the protein being produced, which causes damage to the cells in specific areas of the brain.

Huntington's disease is a debilitating and life-threatening condition because it causes severe behavioural and mental problems, a progressive loss of the ability to move and potentially life-threatening complications.

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

At the time of designation, Huntington's disease affected approximately 1.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 62,000 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 treatments authorised in the EU for Huntington's disease were aimed at relieving the symptoms of the disease. In some Member States, haloperidol, pimozide, tetrabenazine

*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 518,400,000 (Eurostat 2019).

**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

and tiapride were authorised for the abnormal involuntary movements that occur in Huntington's disease. In addition, benzodiazepines were used for anxiety, and antidepressants and lithium to treat depression and mood swings.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Huntington's disease. Laboratory data suggest that the medicine may slow down the loss of ability to move, which is not targeted by current treatments.

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?

A build-up of cholesterol has been observed in brain cells of patients with Huntington's disease. This build-up of cholesterol, which can damage brain cells, is thought to be due to a reduction in the enzyme cholesterol 24-hydroxylase that breaks down cholesterol.

The medicine is made of a virus that contains normal copies of the gene that is responsible for the production of the cholesterol 24-hydroxylase enzyme. When injected into the patient's brain, it is expected that the virus carries the gene into the brain cells, enabling them to produce the enzyme. This is expected to improve symptoms of the disease.

The type of virus used in this medicine (adeno-associated virus) is modified so that it 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, no clinical trials with the medicine in patients with for Huntington's disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Huntington's disease 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 21 February 2019 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 the EMA website.

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 rh10 containing the human cholesterol 24-hydroxylase gene | Treatment of Huntington's disease |
| Bulgarian | Адено-асоцииран вирусен вектор серотип rh10, съдържащ човешкия ген за холестерол 24-хидроксилаза | Лечение на болест на Хънтингтон |
| Croatian | Adeno-pridruženi virusni vektor serotipa rh10 koji sadrži humani gen za kolesterol 24-hidroksilazu | Liječenje Huntingtonove bolesti |
| Czech | Adeno-asociovaný virový vector sérotypu rh10 obsahující lidský gen pro cholesterol 24-hydroxylasu | Léčba Huntingtonovy nemoci |
| Danish | Adeno-associeret viral vector serotype rh10 indeholdende human cholesterol 24-hydroxylase genet | Behandling af Huntington's sygdom |
| Dutch | Adeno-geassociëerde virale vector serotype rh10 welke het humaan cholesterol 24-hydroxylase gen bevat | Behandeling van de ziekte van Huntington |
| Estonian | Inimese kolesterool 24-hüdroksülaasi geeni sisaldav adeno-assotsieerunud viirusvektori serotüüp rh10 | Huntington'i tõve ravi |
| Finnish | Adenoassosioitu serotyypin rh10 virusvektori, joka sisältää ihmisen kolesteroli-24-hydroksylaasigeenin | Huntingtonin taudin hoito |
| French | Vecteur viral adéno-associé de sérotype rh10 contenant le gène humain 24-hydroxylase cholestérol | Traitement de la maladie d'Huntington |
| German | Adeno-assoziierter viraler Vector vom Serotyp rh10, der das humane Cholesterol 24-Hydroxylase Gen enthält | Behandlung der Huntington Erkrankung |
| Greek | Αδενο-σχετιζόμενος ιικός φορέας οροτύπου rh10 περιέχων το ανθρώπινο γονίδιο της 24-υδροξυλάσης της χοληστερόλης | Θεραπεία της νόσου Huntington |
| Hungarian | Humán koleszterin 24-hidroxiláz gént kódoló rh10 szerotípusú adeno-asszociált virus vektor | Huntington kór kezelése |
| Italian | Vettore virale adenoassociato di serotipo rh10 contenente il gene della cholesterol-24 idrolasi umana | Trattamento della malattia di Huntington |
| Latvian | Adeno-associētā vīrusa vektora serotips rh10, kas satur cilvēka holesterola 24-hidroksilāzes gēnu | Hantingtona slimības ārstēšanai |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Lithuanian | Adeno asocijuoto viruso vektoriaus serotipas rh10, pernešantis žmogaus cholesterolio 24-hidroksilazės geną | Huntington’o ligos gydymas |
| Maltese | Serotip tal-vettur virali adeno-assoċjat rh10 li fih il-ġene tal-kolesterol uman 24-hydroxylase | Kura tal-marda ta’ Huntington |
| Polish | Wektor wirusowy związany z adenowirusami serotypu rh10 zawierający ludzki gen 24-hydroksylazy cholesterolu | Leczenie pląsawicy Huntingtona |
| Portuguese | Vetor viral adeno-associado de serotipo rh10 contendo o gene humano da colesterol 24-hidroxilase | Tratamento da doença de Huntington |
| Romanian | Vector viral adeno-asociat de serotip rh10 ce conţina gena umană a cholesterol 24-hidroxilazei | Tratamentul bolii Huntington |
| Slovak | Adeno-asociovaný vírusový vektor sérotypu rh10 obsahujúci ľudský gén pre cholesterol 24-hydroxylázu | Liečba Huntingtonovej choroby |
| Slovenian | Adenovirusom pridruženi vector serotipa rh 10, ki vsebuje gen za humano 24-hidroksilazo holesterola | Zdravljenje Huntingtonove bolezni |
| Spanish | Vector viral adenoasociado de serotipo rh10 que contiene el gen humano de la hidroxilase de cholesterol 24 | Tratamiento de la enfermedad de Huntington |
| Swedish | Adenoassosierad virusvektor serotype rh10 innehållande genen for humant kolesterol-24-hydroxylas | Behandling av Huntingtons sjukdom |
| Norwegian | Adenoassosiert virusvektor serotype rh10 som inneholder genet for humant kolesterol-24-hydroksylase | Behandling av Huntingtons sykdom |
| Icelandic | Adenótengd veiruferja af sermigerð rh10 sem inniheldur kólesteról 24 hýdroxýlasa gen manna | Meðferð við Huntingtons sjúkdómi |