15 May 2018
EMA/184161/2018

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 9 encoding miRNA against human superoxide dismutase 1 for the treatment of amyotrophic lateral sclerosis

On 16 April 2018, orphan designation (EU/3/18/2008) was granted by the European Commission to Stolmàr & Partner Patentanwälte PartG mbB, Germany, for adeno-associated viral vector serotype 9 encoding miRNA against human superoxide dismutase 1 for the treatment of amyotrophic lateral sclerosis.

What is amyotrophic lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. The exact causes are unknown but are believed to include genetic and environmental factors. The symptoms of ALS depend on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, and difficulty speaking, swallowing and breathing. ALS usually starts in mid-life and men are more likely to develop the disease than women.

ALS is a debilitating and life-threatening disease because of the gradual loss of function and its paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure.

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

At the time of designation, ALS affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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, riluzole was authorised in the EU to treat ALS. Patients also received supportive treatment to relieve the symptoms of the disease, such as treatment with baclofen as well as physiotherapy and breathing support.

[*]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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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS. Laboratory studies suggested that the medicine works in a different way to riluzole and baclofen and could lead to improvements in the ability to move. 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?

In some patients with ALS, the condition is caused by a mutation (change) in a gene responsible for producing the enzyme superoxide dismutase 1 (SOD1). This mutation leads to the production of a defective SOD1 which is toxic to nerve cells, eventually causing them to die.

The medicine is made of a virus that contains small fragments of genetic material (RNA) which are expected to interfere with the production of the defective SOD1 protein in nerve cells. This is expected to reduce the production of defective SOD1 and help 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?

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 ALS had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for ALS 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 15 March 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 encoding miRNA against human superoxide dismutase 1	Treatment of amyotrophic lateral sclerosis
Bulgarian	Адено-свързан вирусен вектор серотип 9, кодиращ микро РНК срещу човешка супероксид дисмутаза 1	Лечение на амиотрофична латерална склероза
Croatian	Adeno-vezani virusni vektor serotipa 9 koji kodira miRNA protiv ljudske superoksid dismutaze 1	Liječenje amiotrofične lateralne skleroze
Czech	Adeno-asociovaný virový vektor sérotypu 9 kódující miRNA proti lidské superoxidové dismutáze 1	Léčba amyotrofické laterální sklerózy (ALS)
Danish	Adenoassocieret viral serotype 9 vektor, der koder for miRNA mod human superoxiddismutase 1	Behandling af amyotrofisk lateralsklerose
Dutch	Adeno-geassocieerde virale vector serotype 9 dat codeert voor miRNA tegen humaan superoxide dismutase 1	Behandeling van amyotrofe lateraalsclerose
Estonian	Inimese superoksiid-dismutaas 1 vastast miRNA-d kodeeriv adeno-assotsieerunud viirusvektori serotüüp 9	Amüotroofilise lateraalskleroosi ravi
Finnish	Adenoassosioitu virusvektori, serotyyppiä 9, joka koodaa miRNA: ta ihmisen superoksididismutaasi 1:tä vastaan	Amyotrofisen lateraaliskleroosin hoito
French	Vecteur viral adéno-associé de sérotype 9 codant pour un micro ARN dirigé contre la superoxyde dismutase 1	Traitement de la sclérose latérale amyotrophique
German	Adeno-assoziierter viraler Vektor vom Serotyp 9, der für eine miRNA gegen humane Superoxid dismutase 1 kodiert	Behandlung der amyotrophen Lateralsklerose
Greek	Αδενοσχετιζόμενος ιικός φορέας οροτύπου 9 που κωδικοποιεί ένα miRNA κατά της ανθρώπινης δισμουτάσης υπεροξειδίου 1	Θεραπεία πλάγιας μυοατροφικής σκλήρυνσης
Hungarian	Humán szuperoxid-diszmutáz 1 elleni miRNS-t kódoló 9-es szerotípusú adeno-asszociált vírus vektor	Amyotrophiás lateral sclerosis kezelése
Italian	Vettore virale adeno-associato di sierotipo 9 che codifica il miRNA attivo contro la superossido dismutasi umana 1	Trattamento della sclerosi laterale amiotrofica
Latvian	Adeno-saistītā vīrālā vektora 9. serotips, kas kodē miRNS pret cilvēka superoksīddismutāzi 1	Amiotrofiskās laterālās sklerozes ārstēšana
Lithuanian	Adeno asocijuoto viruso vektoriaus 9 serotipas, koduojantis miRNR prieš žmogaus superoksido dismutazę 1	Šoninės amiotrofinės sklerozės gydymas
Maltese	Vettur virali tas-serotip 9 assoċjat ma' adeno kodifikazzjoni miRNA kontra dismutaži 1 superossidu uman	Kura tas-sklerosi laterali amjotrofika

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Wektor wirusowy związany z adenowirusami serotypu 9 kodujący miRNA przeciwko ludzkiej dysmutazie ponadtlenkowej 1	Leczenie stwardnienia bocznego zanikowego
Portuguese	Vetor viral adeno-associado de serotipo 9 codificando um miRNA contra a superóxido dismutase humana 1	Tratamento da esclerose lateral amiotrófica
Romanian	Vector viral adeno-asociat de serotip 9 care codifică miRNA împotriva superoxid dismutazei umane 1	Tratamentul sclerozei laterale amiotrofice
Slovak	Adeno-asociovaný vírusový vektor sérotypu 9 kódujúci miRNA proti ľudskej superoxiddismutáze 1	Liečba amyotrofickej laterálnej sklerózy
Slovenian	Adeno-pridruženi virusni vektor serotipa 9, ki kodira miRNK proti humanisuperoksid dismutazi 1	Zdravljenje amiotrofične lateralne skleroze
Spanish	Vector viral adenoasociado recombinante serotipo 9 que codifica el miARN contra la superóxido dismutasa humana 1	Tratamiento de la esclerosis lateral amiotrófica
Swedish	Adenoassocierad virusvektor serotyp 9 som kodar för miRNA mot humant superoxiddismutas 1	Behandling av amyotrofisk lateralskleros
Norwegian	Adenoassosiert virusvektor serotype 9 som koder for miRNA mot human superoksiddismutase 1	Behandling av amyotrofisk lateralsklerose
Icelandic	Adenótengd veiruferja af sermisgerð 9 sem kóðar fyrir miRNA gegn manna superoxíð dismútasa 1	Meðferð við blandaðri hreyfitaugahrörnun