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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Genetically modified adeno-associated viral vector serotype 9 expressing shRNA as well as a codon-optimised shRNA-insensitive wildtype PABPN1 for the treatment of oculopharyngeal muscular dystrophy

On 12 January 2017, orphan designation (EU/3/16/1816) was granted by the European Commission to Clinipace GmbH, Germany, for genetically modified adeno-associated viral vector serotype 9 expressing shRNA as well as a codon-optimised shRNA-insensitive wildtype PABPN1 (also known as BB-301) for the treatment of oculopharyngeal muscular dystrophy.

What is oculopharyngeal muscular dystrophy?

Oculopharyngeal muscular dystrophy is a hereditary condition marked by weakness of the muscles around the eyes and throat, leading to symptoms such as drooping eyelids and difficulty swallowing. As muscle weakness progresses, weakness in other parts of the body may also develop, particularly in the arms near the shoulder and in the upper legs and hips. Patients usually present with this condition in their sixties or seventies.

The condition is caused by a mutation (change) in the gene that produces a protein called PABPN1. In patients with the mutation, an abnormal form of PABPN1 is produced, which builds up in muscle cells and stops muscles working properly.

Oculopharyngeal muscular dystrophy is debilitating in the long term because of its symptoms such as drooping eyelids and difficulty swallowing, and because it spreads to other parts of the body affecting mobility.

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

At the time of designation, oculopharyngeal muscular dystrophy affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 5,000 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).

[*]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 submission of the application for orphan drug designation, there were no satisfactory treatments authorised for the condition. Patients were mainly treated with speech therapy, physiotherapy and surgery to help with drooping eyelids and swallowing difficulty.

How is this medicine expected to work?

This medicine consists of a virus that has been modified to contain genetic material that replaces the defective PABPN1 gene, together with other genetic material that stops the patient's defective gene from working. When given to patients, the virus is expected to carry the genetic material into muscle cells of the oesophagus (the tube that leads from the mouth to the stomach).

This would enable these muscle cells to produce the normal form of PABPN1 and stops production of abnormal PABPN1. Together, these effects are expected to improve muscle strength and thereby relieve symptoms affecting the oesophagus.

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 oculopharyngeal muscular dystrophy had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for oculopharyngeal muscular dystrophy 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 8 December 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	Genetically modified adeno-associated viral vector serotype 9 expressing shRNA as well as a codon-optimized shRNA-insensitive wildtype PABPN1	Treatment of oculopharyngeal muscular dystrophy
Bulgarian	Генетично модифициран, адено-свързан вирусен вектор, серотип 9, експресиращ къса синтетична РНК (shRNA), както и кодон-оптимизиран, нечувствителен към shRNA, див тип PABPN1	Лечение на окулофарингеална мускулна дистрофия
Croatian	Genetički modificiran adeno-vezani virusni vektor serotpa 9 koji izražava shRNK, kao i PABPN1 divljeg tipa, neosjetljiv na shRNK s optimiziranim kodonom	Liječenje okulofaringealne mišićne distrofije
Czech	Geneticky modifikovaný adeno-asociovaný virální vektor sérotyp 9 exprimující shRNA, jakož i kodonově optimalizovaný, shRNA nesenzitivní, divoký í gen PABPN1	Léčba oculofaryngealní muskulární dystrofie
Danish	Genetisk modificeret adeno-associeret virus serotype AAV9, der udtrykker shRNA, samt et codonoptimeret, shRNA-ufølsomt, vildtype PABPN1	Behandling af oculopharyngeal muskeldystrofi
Dutch	Genetisch gemodificeerd adenogeassocieerde virale vector serotype 9 dat zowel shRNA als een codon-geoptimaliseerd, shRNA-ongevoelig wildtype-PABPN1 tot expressie brengt	Behandeling van oculofaryngeale spierdystrofie
Estonian	Geneetiliselt muundatud adenoassotsieerunud viirusvektori serotüüp 9, mis ekspresseerib shRNA-d ning ka koodonoptimeeritud shRNA-le tundetut metsiktüüpi PABPN1	Okulofarüngeaalse lihasdüstroofia ravi
Finnish	Geenimuunneltu AA-virusvektori serotyyppi 9, joka ilmentää shRNA:ta samoin kuin kodonioptimoitua, shRNA-insensitiivistä, villityypin PABPN1-geeniä	Okulofaryngeaalisen lihasdystrofian hoito
French	Vecteur viral adéno-associé génétiquement modifié de sérotype 9 exprimant un shARN ainsi qu'une PABPN1 de type sauvage, insensible au shARN, à codon optimisé	Traitement de la dystrophie musculaire oculopharyngée
German	Genetisch verändertes Adeno-assoziiertes Virus vom Serotyp AAV9, das für eine shRNA und für Codon-optimiertes, shRNA-unempfindliches, Wildtyp-PABPN1 codiert	Behandlung der okulopharyngealen Muskeldystrophie
Greek	Γενετικά τροποποιημένος αδενο-συσχετιζόμενος ιός οροτύπου 9 που εκφράζει shRNA καθώς και ένα βελτιστοποιημένων κωδικονίων, μη ευαίσθητο στο shRNA, PABPN1 μη μεταλλαγμένου τύπου	Θεραπεία της οφθαλμοφαρυγγικής μυϊκής δυστροφίας
Hungarian	Genetikailag módosított, shRNS-t és kodonoptimalizált, shRNS iránt nem érzékeny, vad típusú PABPN1-et expresszáló adenoasszociált 9-es szerotípusú virus vector	Oculopharyngealis izomsorvadás kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Virus adeno-associato geneticamente modificato del sierotipo 9, esprimente shRNA e un gene PABPN1 non mutato con codoni ottimizzati, insensibile a shRNA	Trattamento della distrofia muscolare oculofaringea
Latvian	Ģenētiski modificēts 9. serotipa adeno-asociētā vīrusa vektors, kas ekspresē shRNS kā arī pret shRNS nejutīgu savvaļas tipa PABPN1 ar optimizētu kodonu	Okulofaringeālās muskuļu distrofijas ārstēšana
Lithuanian	Genetiškai modifikuotas su adenovirusu susijusio 9 serotipo vektorius, ekspresuojantis shRNR, taip gerai, kaip kodono-optimizuotas shRNR-nejautrus laukinis tipas PABPN1	Akių ir ryklės (okulofaringealinės) raumenų distrofijos gydymas
Maltese	Vettur virali modifikat ġenetikament assoċjat ma' adeno serotip 9 li jesprimi kemm shRNA kif ukoll PABPN1 tat-tip salvaġġ ottimizzat permezz ta' kodon u insensittiv għal shRNA	Kura tad-distrofija muskolari okulofaranġili
Polish	Genetycznie zmodyfikowany wirus związany z adenowirusami serotypu 9, eksprymujący shRNA jak również niewrażliwy na shRNA gen PABPN1 typu dzikiego ze zoptymalizowanym kodonem	Leczenie dystrofii mięśniowej oczno-gardzielowej
Portuguese	Vetor viral adeno-associado de serotipo 9 geneticamente modificado que expressa um shRNA assim como um codão shRNA-insensível de tipo selvagem PABPN1 optimizado	Tratamento da distrofia muscular oculofaríngea
Romanian	Vector viral adeno-asociat de serotip 9 modificat genetic, care exprimă ARNss, precum și o genă PABPN1 de tip sălbatic cu codoni optimizați, insensibilă la ARNss	Tratamentul distrofiei musculare oculofaringiene
Slovak	Geneticky modifikovaný adeno-asociovaný vírusový vektor sérotypu 9 exprimujúci shRNA a gén PABPN1 divokého typu s optimalizovanými kodónmi necitlivý na shRNA	Liečba oculopharyngealnej muskulárnej dystrofie
Slovenian	Gensko spremenjeni adenovirusom pridruženi virus serotip 9, ki izraža shRNA in s kodonom optimiran, na shRNA neobčutljiv, PABPN1 divjega tipa	Zdravljenje okulofaringealne mišične distrofije
Spanish	Adenovirus de serotipo 9 genéticamente modificado que expresa shRNA así como un tipo salvaje de PABPN1, optimizado por codón, insensible a shRNA	Tratamiento de la distrofia muscular oculofaríngea
Swedish	Genmodifierat Adeno-associerat virusvektor av serotyp 9 som uttrycker shRNA liksom ett kodonoptimerat, shRNA-okänsligt vildtyps-PABPN1	Behandling av oculopharyngeal muskeldystrofi
Norwegian	Genmodifisert adenoassosiert virusvektor serotype 9 som uttrykker shRNA samt kodonoptimalisert villtype PABPN1 som er insensitiv mot shRNA	Behandling av okulofaryngeal muskeldystrofi
Icelandic	Erfðabreytt adenótengd veira sermsigerð 9 sem tjáir shRNA sem og shRNA-ónæma villigerð af PABPN1 með hámarkstáknun	Meðferð augn-og kok vöðvarýrnunar