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Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector containing a bioengineered capsid derived from AAV-rh74 and a codon-optimised expression cassette to drive the expression of a secretable form of human acid alpha-glucosidase for the treatment of glycogen storage disease type II (Pompe's disease)

On 28 June 2019 orphan designation EU/3/19/2175 was granted by the European Commission to Spark Therapeutics Ireland Limited, Ireland, for recombinant adeno-associated viral vector containing a bioengineered capsid derived from AAV-rh74 and a codon-optimised expression cassette to drive the expression of a secretable form of human acid alpha-glucosidase (also known as SPK-3006) for the treatment of glycogen storage disease type II (Pompe's disease).

What is glycogen storage disease type II (Pompe's disease)?

Glycogen storage disease type II, also known as Pompe's disease, is an inherited disorder caused by the lack of an enzyme called acid alpha-glucosidase (GAA). This enzyme is contained in lysosomes (part of the body's cells that break down nutrients and other materials). GAA breaks down glycogen (a complex sugar stored in the body) into glucose (a simple sugar). When this enzyme is lacking, large amounts of glycogen build up in the muscles, including the heart and diaphragm (the main breathing muscle under the lungs). The progressive build-up of glycogen causes a wide range of signs and symptoms, including heart problems, breathing difficulties and muscle weakness.

Glycogen storage disease type II is a long-term debilitating and life-threatening disease because it causes breathing and heart problems and is associated with premature death.

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

At the time of designation, glycogen storage disease type II affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 16,000 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 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

What treatments are available?

At the time of designation, Myozyme (alglucosidase alfa) was authorised for the treatment of glycogen storage disease type II in the EU. Myozyme is an 'enzyme replacement therapy' that works by replacing the missing GAA enzyme.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with glycogen storage disease type II because laboratory studies suggested that a single dose of the medicine could increase GAA activity for a long period and improve muscle strength. 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 made of a virus that has been modified to contain the GAA gene. When injected into the patient, the virus is expected to carry the gene into the liver cells, enabling them to start producing the GAA enzyme, which is then carried around the body. This is expected to replace the missing GAA and break down and reduce the build-up of glycogen, thereby improving the symptoms of the disease.

The type of virus used in this medicine (adeno-associated virus) does not cause viral 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 of the application for orphan designation, no clinical trials with the medicine in patients with glycogen storage disease type II had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of glycogen storage disease type II. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 23 May 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 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	Recombinant adeno-associated viral vector containing a bioengineered capsid derived from AAV-rh74 and a codon-optimised expression cassette to drive the expression of a secretable form of human acid alpha-glucosidase	Treatment of glycogen storage disease type II (Pompe's disease)
Bulgarian	Рекомбинантен адено-асоцииран вирусен вектор, съдържащ обработен по биотехнологичен метод капсид, получен от AAB rh74 и кодон-оптимизирана експресионна касета за стимулиране на експресията на секретируема форма на човешка киселa α-глюкозидаза	Лечение на тип 2 гликогеноза (Болест на Помпе)
Croatian	Rekombinantni adeno-povezani virusni vektor koji sadrži kapsid dobiven bioinženjeringom iz AAV-rh74 i ekspresijsku kazetu optimiziranu kodonom da se potakne ekspresija oblika ljudske kisele α-glukozidaze koji se može izlučiti	Liječenje bolesti taloženja glikogena tip II (Pompeova bolest)
Czech	Rekombinantní adeno-asociovaný virový vektor obsahující bioinženýrsky zpracovanou kapsidu odvozenou od AAV-rh74 a kodonově optimalizovanou expresní kazetu pro řízení exprese sekreční formy lidské kyselé α-glukosidázy	Léba glykogenózy typu II (Pompeho choroba)
Danish	Rekombinant adenoassocieret viral vektor indeholdende et bioteknologisk fremstillet capsid deriveret fra AAV-rh74 og en kodonoptimeret ekspressionskassette til at stimulere ekspressionen af en secernerbar form af human sur α-glucosidase	Behandling af glycogenose type II (Pompes sygdom)
Dutch	Recombinant-adenogeassocieerde virale vector die een door biotechnologie verkregen capside afkomstig van AAV rh74 en een codon-geoptimaliseerde expressiecassette bevat om de expressie van een uitscheidbare vorm van humaan zure α glucosidase te bevorderen	Behandeling van de glycogeenstapelingsziekte type II (Pompe-ziekte)
Estonian	Biotehnoloogiliselt valmistatud AAV-rh74-päritolu kapsiidi ja koodon-optimeeritud ekspressioonikassetti sisaldav rekombinantne adeno-seoselise viiruse vektor inimese happelise α-glükosidaasi sekreteeriva vormi ekspressiooni saavutamiseks	2.tüüpi glükogenoosi (Pompe tõve) ravi

[1] At the time of designation

Language	Active ingredient	Indication
Finnish	Rekombinantti adenoassosioitu virusvektori, jossa on ka sisältää bioteknisesti rakennettun kapsidin AAV-rh74:stä ja kodonioptimoidtun ekspressiokasettin ohjaamaan ihmisen happaman α-glukosidaasin eritettävän	Tyyppi II glykogenoosin (Pompen tauti) hoito
French	Vecteur viral AAV (adeno associated virus - virus adéno associé) recombinant contenant une capside produite par bio ingénierie dérivée de l'AAV rh74 et une cassette d'expression optimisée par codons pour induire l'expression d'une forme sécrétable d'alpha-glucosidase acide humaine	Traitement de la glycogénose de type II (maladie de Pompe)
German	Rekombinanter Adeno-assoziierter viraler Vektor, der ein biotechnologisch hergestelltes Kapsid vom Serotyp AAV rh74 und eine Codon-optimierte Expressionskassette zur Steuerung der Expression einer sezernierbaren Form der humanen sauren α-Glucosidase enthält	Behandlung der Glykogenspeicherkrankheit Typ II (Pompe-Krankheit)
Greek	Ανασυνδυασμένος αδενοσχετιζόμενος ιικός φορέας που περιέχει βιο-κατασκευασμένο καψίδιο προερχόμενο από τον AAV-rh74 και κασέτα έκφρασης βελτιστοποιημένη ως προς τα κωδικόνια για να επάγει την έκφραση μιας εκκρινόμενης μορφής της ανθρώπινης όξινης α-γλυκοσιδάσης	Θεραπεία της Γλυκογόνωσης τύπου II (Νόσος του Pompe)
Hungarian	AAV rh74-ből biotechnológiai módszerrel előállított kapszidot és a humán savi α glükozidáz szekretálható formája expressziójának vezérlésére egy kodon-optimalizált expressziós kazettát tartalmazó rekombináns adeno asszociált vírusvektor	II-es típusú glikogéntárolási betegség (Pompe-kór) kezelése
Italian	Vettore virale adeno-associato ricombinante contenente un capside bioingegnerizzato derivato da AAV-rh74 e una cassetta di espressione con codoni ottimizzati, per promuovere l'espressione di una forma secernibile di α-glucosidasi acida umana	Trattamento della glicogenosi, tipo II (malattia di Pompe)
Latvian	Rekombinants adenoasociēts vīrusa vektors, kas satur ar bioinženieriju radītu kapsīdu, kas iegūts no AAV-rh74, un ekspresijas kaseti ar optimizētu kodonu, lai stimulētu cilvēka skābās α-glikozidāzes sekretējamas formas ekspresiju	Glikogēna uzkrāšanas II tipa traucējumu (Pompe slimība) ārstēšana
Lithuanian	Rekombinantinis adeno asocijuotojo viruso vektorius su biologinės inžinerijos būdu sukonstruota kapside, gauta iš AAV rh74, ir kodonų optimizuota raiškos kasetė, sekretuojamos žmogaus rūgštinės α gliukozidazės formos raiškai sužadinti	II tipo glikogenozės (Pompe ligos) gydymas

Language	Active ingredient	Indication
Maltese	Vettur virali rikombinanti assoċjat ma' adeno li fih kapsida tal-bijoinġinerija dderivata minn AAV-rh74 u expression cassette ottimizzat minn kodon biex imexxi l-espressjoni ta' forma ta' sekrezzjoni ta' aċidu α-glukosidaži. uman	Kura tal-glikoġenoży tat-tip II (marda ta' Pompe)
Polish	Rekombinowany wektor wirusowy związany z adenowirusami kodujący modyfikowany metodami inżynierii genetycznej kapsyd pozyskany z wirusa AAV rh74 oraz kasetę ekspresyjną zoptymalizowaną pod względem wykorzystania kodonów, która wyraża wydzielniczą formę ludzkiej alfa glukozydazy.	Leczenie choroby spichrzania glikogenu typu II (choroby Pompego)
Portuguese	Vetor viral recombinante adeno-associado contendo uma cápside derivada de AAV-rh74, concebida por bioengenharia, e uma cassette de expressão de codão otimizada para promover a expressão de uma forma secretável da α-glucosidase ácida humana	Tratamento da glicogenose de tipo II (Doença de Pompe)
Romanian	Vector viral adeno-asociat recombinant care conține o capsidă produsă prin bioinginerie derivată din AAV-rh74 și o casetă de exprimare cu optimizarea codonilor pentru a stimula exprimarea unei forme secretabile de α glucozidază acidă umană	Tratamentul glicogenozei tip II (boala Pompe)
Slovak	Rekombinantný adeno-asociovaný vírusový vektor obsahujúci bioinžiniersky vytvorený kapsid odvodený od AAV rh74 a kodónovo optimalizovanú expresnú kazetu na riadenie expresie sekrečnej formy ľudskej kyslej α-glukozidázy	Liečba glykogenózy typ II (Pompeho choroba)
Slovenian	Rekombinantni virusni vektor, povezan z adenovirusom, ki vsebuje z bioinženiringom pridobljeno kapsido, izpeljano iz AAV-rh74, in za kodon optimizirano ekspresijsko kaseto za izvedbo ekspresije sekretabilne oblike človeške kisle α-glukozidaze.	Zdravljenje glikogenoze tipa II (Pompejeva bolezen)
Spanish	Vector viral adenoasociado recombinante que contiene una cápside derivada de AAV-rh74 elaborada mediante biotecnología y un casete de expresión optimizado para codones para impulsar la expresión de una forma segregable de la α-glucosidasa ácida humana	Tratamiento de la enfermedad de almacenamiento del glucógeno tipo II (enfermedad de Pompe)
Swedish	Rekombinant adenoassocierad virusvektor innehållande en biotekniskt framställd kapsid med ursprung i AAV-rh74 och en kodonoptimerad uttryckskassett för att driva uttrycket för en utsöndringsbar form av humant surt alfaglukosidas	Behandling av glykogen upplagringssjukdom typ II (Pompes sjukdom)

Language	Active ingredient	Indication
Norwegian	Rekombinant adenoassosiertrelatert virusal vektor som inneholdernde et bioteknologisk fremstilt kapsid derivert fra AAV-rh74 og en kodonoptimalisert ekspresjonskassett for å som driver ekspresjonen av en utskillbar form av human syre-α-glukosidase	Behandling av glykogenose type II (Pompes sykdom)
Icelandic	Raðbrigða adenótengd veiruferja sem inniheldur líftæknilegan veiruhjúp sem afleiddur er úr AAV-rh74 og táknahámarkaða tjáningarkassettu til að knýja tjáningu á seytanlegu formi sýru α-glúkósídasa hjá mönnum	Meðferð á glýkógenupphleðslu sjúkómi af gerð II (Pompes sjúkdómur)