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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 8 encoding the human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter for the treatment of Wilson's disease

On 11 November 2015, orphan designation (EU/3/15/1573) was granted by the European Commission to Aligen Therapeutics S.L., Spain, for adeno-associated viral vector serotype 8 encoding the human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter for the treatment of Wilson's disease.

What is Wilson's disease?

Wilson's disease is a genetic disorder that causes copper absorbed from food to accumulate in the body. In healthy people, liver cells remove most of the excess copper and release it into the bile, which flows into the intestines. In people with Wilson's disease, due to a genetic mutation (change), the liver cannot remove copper and the copper builds up in the liver and in other organs such as the kidneys, brain and eyes, and damages them.

Wilson's disease is chronically debilitating and can be life threatening if not treated due to the toxicity of copper in the liver and brain.

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

At the time of designation, Wilson's disease affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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, several medicines were authorised in the EU for the treatment of Wilson's disease. Penicillamine and trientine were used to remove excess copper from the body and to limit the

[*]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 512,900,000 (Eurostat 2015).

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absorption of copper from food. Trientine was authorised for patients who cannot take penicillamine, but it was authorised in one EU country only. Zinc, which reduces the absorption of copper from food, was also authorised for Wilson's disease.

The sponsor has provided sufficient information to show that the medicine, adeno-associated viral vector serotype 8 encoding the human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter, might be of significant benefit for patients with Wilson's disease because it is expected to work in a different way to existing treatments to correct the underlying problem with the way the liver removes copper from the body. 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?

Because of a genetic mutation, in patients with Wilson's disease a protein in liver cells called ATP7B does not work properly. As a result, the liver cannot remove copper.

The medicine is made of a virus that has been modified to contain normal copies of the gene for the ATP7B protein. After being given to the patient as an injection into a vein, the virus is expected to carry the *ATP7B* gene into the liver cells, enabling them to produce a functional protein. This is expected to correct how the body handles copper.

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 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 Wilson's disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Wilson'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 8 October 2015 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 8 encoding the human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter	Treatment of Wilson's disease
Bulgarian	Адено-свързан вирусен вектор, серологичен тип 8, кодиращ човешкия ATP7B ген под контрола на промотера на човешкия алфа-1 антитрипсин	Лечение на болест на Уилсън
Croatian	Adeno-povezani virusni vektor serotipa 8 koji kodira za ljudski gen *ATP7B* pod kontrolom ljudskog promotora α1-anti-tripsina	Liječenje Wilsonove bolesti
Czech	Vektor odvozený z adeno-asociovaného viru sérotyp 8, kódující lidský ATP7B kontrolovaný promotorem lidského jaterního α1-anti-trypsinu	Léčba Wilsonovy choroby
Danish	Adenoassocieret vektorserotype 8, der koder for-humant *ATP7B*-genet placeret under kontrol af human, lever-specifik α1-anti-trypsin-promoter	Behandling af Wilsons sygdom
Dutch	Adeno-geassocieerde vector van serotype 8 die codeert voor het humaan *ATP7B* gen dat onder controle staat van de humane alpha-1 antitrypsine promotor	Behandeling van de ziekte van Wilson
Estonian	Adenoviirusega seotud viirusvektori serotüüp 8, mis kodeerib inimese ATP7B geeni, mis on inimese α1-antitrüpsiin promootori kontrolli all	Wilsoni haiguse ravi
Finnish	Serotyypin 8 adenovirusvektori, joka koodaa ihmisen α1-antitrypsiinipromoottorin kontrolloimaa ihmisen ATP7B:n geeniä	Wilsonin taudin hoito
French	Vecteur viral adéno-associé de sérotype 8 qui code le gène humain ATP7B placé sous le contrôle du promoteur de l'alpha-1 antitrypsine humaine	Traitement de la maladie de Wilson
German	Adeno-assoziierter Vektor vom Serotyp 8, welcher unter der Kontrolle des a1-Anti-Trypsin Promotor das humane ATP7B kodiert	Behandlung des Morbus Wilson
Greek	Αδενοσυσχετιζόμενος ιικός φορέας οροτύπου 8 που κωδικοποιεί το ανθρώπινο γονίδιο *ATP7B*, υπό τον έλεγχο του ανθρώπινου υποκινητή α1-αντι-θρυψίνης	Θεραπεία της νόσου του Wilson
Hungarian	8-as szerotípusú adeno-asszociált vírus vektor, amely a humán alfa-1 antitripszin promóter kontrollált humán ATP7B gént kódolja	Wilson-betegség kezelése
Italian	Vettore adenovirale di sierotipo 8 codificante il gene umano ATP7B posto sotto il controllo del promotore della alfa-1-antitripsina	Trattamento del morbo di Wilson

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Adenoasociēts vīrusa vektora serotips 8, kas kodē cilvēka ATP7B gēnu, kam noteikta cilvēka alfa-1 antitripsīna veicinātāja kontrole	Vilsona slimības ārstēšana
Lithuanian	Su adenovirusu susijusio virusinio vektoriaus 8 serotipas, koduojantis žmogaus *ATP7B* geną, kontroliuojamą žmogaus α1-antitripsino promotoriaus	Vilsono ligos gydymas
Maltese	Vettur imnissel mill-adenovirus tas-serotip 8 li jikkodifika il-ġene ATP7B uman ikkontrollat mill-promotur tal-alpha-1 antitrypsin uman	Kura tal-marda ta' Wilson
Polish	Wirus związany z adenowirusami serotyp 8 kodujący ludzki gen ATP7B pod kontrolą promotora Alfa1-antytrypsyny	Leczenie choroby Wilsona
Portuguese	Vetor adeno-associado de serótipo 8 que codifica o ADN complementar do gene ATP7B humano sob o controlo do promotor da alfa-1-antitripsina humana	Tratamento da doença de Wilson
Romanian	Vector viral adeno-asociat de serotip 8 care codifică gena umană ATP7B cDNA pusă sub controlul promotorului de α1-antitripsină umană	Tratamentul bolii Wilson
Slovak	Adeno-asociovaný vektor sérotypu 8 kódujúci ľudský ATP7B gén pod kontrolu ľudského stimulátora α1-anti-trypsínu	Liečba Wilsonovej choroby
Slovenian	Adeno-pridruženi virusni vektor serotipa 8, ki kodira humani ATP7B gen, pod nadzorom humanega alfa-1 antitripsinskega promotorja	Zdravljenje Wilsonove bolezni
Spanish	Vector viral adenoasociado de serotipo 8 que codifica el ADN complementario del gen ATP7B humano colocado bajo el control del promotor de la alfa-1-antitripsina humana como promotor específico del hígado	Tratamiento de la enfermedad de Wilson
Swedish	Adeno-associerad viral vektor serotyp 8 koderad för den humana ATP7B genen under kontroll av den humana lever- specifika α1-anti-trypsin promotorn	Behandling av Wilsons sjukdom
Norwegian	Adenoassosiert vektorserotype 8 som kartlegger menneskelig ATP7B cDNA under kontroll av den menneskelige leverspesifikke α1-anti-trypsin-agonisten	Behandling av Wilsons sykdom
Icelandic	Adenótengd veiruferja sermisgerð B sem kóðar fyrir manna ATP7B geni undir stjórn manna alfa-1 antitrýpsín hvata	Meðferð við Wilsons sjúkdómi