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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype Anc80 containing the truncated human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter for the treatment of Wilson's disease

On 23 August 2017, orphan designation (EU/3/17/1898) was granted by the European Commission to Vivet Therapeutics SAS, France, for adeno-associated viral vector serotype Anc80 containing the truncated human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter (also known as VTX-801) 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 excess copper. In people with Wilson's disease, due to a genetic mutation (change), the liver cannot remove copper, which builds up in the liver and in other organs such as the brain, 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, penicillamine, trientine and zinc acetate were authorised in the EU for the treatment of Wilson's disease. The only curative treatment for Wilson's disease was liver transplantation.

*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 515,700,000 (Eurostat 2017).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Wilson's disease, with laboratory studies showing that it replaces the defective gene causing the disease and leads to lasting improvements. It also has the potential to reverse liver damage that has already taken place.

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 functioning 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 13 July 2017 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, 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 Anc80 containing the truncated 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 Anc80, съдържащ скъсен човешки *ATP7B* ген под контрола на промотера на човешкия алфа-1 антитрипсин	Лечение на болест на Уилсън
Croatian	Adeno-povezani virusni vektor serotipa Anc80 koji sadrži skraćeni humani *ATP7B* gen pod kontrolom promotora humanog alfa-1 antitripsina	Liječenje Wilsonove bolesti
Czech	Adeno-asociovaný virový vector serotypu Anc80 obsahující zkrácený lidský gen *ATP7B* kontrolovaný promotorem lidského alfa-1 antitrypsinu	Léčba Wilsonovy choroby
Danish	Adeno-associeret viral vektor serotype Anc80, indeholdende det trunkerede humant *ATP7B* gen, som er under kontrol af human alpha-1 antitrypsin promotoren	Behandling af Wilsons sygdom
Dutch	Adeno-geassociëerde virale vector serotype Anc80 welke getrunceerd humaan *ATP7B* gen bevat onder de controle van de humane alpha-1 antitrypsine promoter	Behandeling van de ziekte van Wilson
Estonian	Lühendatud inimese *ATP7B* geeni sisaldav adenoviirusega assotseerunud viirusvektor serotüüp AncC80, mis on inimese alfa-1 antitrüpsiini promootori kontrolli all	Wilsoni haiguse ravi
Finnish	Adenoassosioitu virusvektori, serotyyppi Anc80, joka sisältää ihmisen alfa-1 antitrypsiini promoottorin säätelemän, typistetyn ihmisen *ATP7B* geenin	Wilsonin taudin hoito
French	Vecteur viral adéno-associé de sérotype Anc80 qui contient le gène humain codé *ATP7B* placé sous le contrôle du promoteur de l'alpha-1 antitrypsine humaine	Traitement de la maladie de Wilson
German	Adeno assoziierter viraler Vektor Serotyp Anc80, der das gekürzte humane *ATP7B* Gen enthält unter der Kontrolle des humanen Alpha-1 Antitrypsin Promoters	Behandlung des Morbus Wilson
Greek	Αδενο-σχετιζόμενος ιϊκός φορέας οροτύπου Anc80 που περιέχει ένα περικομμένο ανθρώπινο *ATP7B* γονίδιο υπό τον έλεγχο του προαγωγέα της ανθρώπινης α-1 αντιθρυψίνης	Θεραπεία της νόσου του Wilson

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	A humán alfa-1 antitripszin promoter kontrollja alatt álló csonkított humán *ATP7B* gént tartalmazó, Anc80 szerotípusú adeno-asszociált vírus vektor	Wilson-betegség kezelése
Italian	Vettore virale adeno-associato di serotipo Anc80 contenente il gene umano troncato *ATP7B* sotto il controllo del promotore dell' alfa-1 antitripsina umana	Trattamento del morbo di Wilson
Latvian	Adeno-asociētā vīrusa Anc80 serotipa vektors, kas satur saīsinātu cilvēka *ATP7B* gēnu, kuru kontrolē cilvēka alfa-1 antitripsīna promoters	Vilsona slimības ārstēšana
Lithuanian	Adenoasocijuoto viruso vektoriaus serotipas Anc80, turintis sutrumpintą žmogaus *ATP7B* geną, reguliuojamą žmogaus alfa-1 antitripsino promotoriaus	Vilsono ligos gydymas
Maltese	Vettur virali serotip Anc80 assoċjat maʾ Adeno li fih il-ġene uman *ATP7B* maqtugħ taħt il-kontroll tal-promotur uman alfa-1 antitripsina	Kura tal-marda ta' Wilson
Polish	Wektor wirusowy związany z adenowirusami serotypu Anc80 zawierający skrócony wariant ludzkiego genu *ATP7B* pod kontrolą promotora ludzkiej antytrypsyny alfa-1	Leczenie choroby Wilsona
Portuguese	Vetor viral adeno-associado de serotipo Anc80 contendo o gene *ATP7B* humano truncado sob o controle do promotor da alfa-1 antitripsina humana	Tratamento da doença de Wilson
Romanian	Vector viral adeno-asociat de serotip Anc80 ce conţine gena umană trunchiată *ATP7B* plasată sub controlul promotorului alfa-1 antitripsinei umane	Tratamentul bolii Wilson
Slovak	Adeno-asociovaný vírusový vektor sérotypu Anc80 obsahujúci skrátený ľudský *ATP7B* gén regulovaný ľudským alfa-1 antitrypsínovým promótorom	Liečba Wilsonovej choroby
Slovenian	Adenovirusom pridruženi virusni vektor serotipa Anc80, ki vsebuje skrajšan humani gen *ATP7B* pod nadzorom promotorja humanega alfa-1 antitripsina	Zdravljenje Wilsonove bolezni
Spanish	Vector viral adeno asociado de serotipo Anc80 codificado que contiene el gen humano *ATP7B* truncado que esta bajo el control del promotor humano antitripsina alfa 1	Tratamiento de la enfermedad de Wilson
Swedish	Adeno-associerad viral vektor av serotyp Anc80 innehållande trunkerad human *ATP7B* gen under kontroll av human alpha-1 antitrypsin promotor	Behandling av Wilsons sjukdom
Norwegian	Adeno-assosiert viral vektor serotype Anc80 inneholdende det trunkerte humane *ATP7B* genet under kontroll av den humane alpha-1 antitrypsin promotoren	Behandling av Wilsons sykdom
Icelandic	Adeno-tengdur veiru vektor sermisgerð An80 sem inniheldur stýft manna *ATP7B* gen undir stjórn manna alfa-1 anti trypsin örva	Meðferð við Wilsons sjúkdómi