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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector of serotype 5 containing the human alanine-glyoxylate aminotransferase gene for the treatment of primary hyperoxaluria type 1

On 21 March 2012, orphan designation (EU/3/12/974) was granted by the European Commission to Amsterdam Molecular Therapeutics BV, the Netherlands, for adeno-associated viral vector of serotype 5 containing the human alanine-glyoxylate aminotransferase gene for the treatment of primary hyperoxaluria type 1.

In July 2012, Amsterdam Molecular Therapeutics BV changed name to uniQure biopharma B.V.

What is primary hyperoxaluria type 1?

Primary hyperoxaluria type 1 is an inherited disease caused by the lack of a liver enzyme called alanine-glyoxylate aminotransferase (AGXT). This enzyme is needed to convert a compound called glyoxylate into glycine (an amino acid), which is used for making enzymes and other proteins. Patients who lack this enzyme have high levels of oxalate in the urine, because glyoxylate instead of being converted into glycine is converted into excess oxalate. Oxalate can form calcium oxalate deposits, which can cause stones in the kidney and urinary tract (structures that carry urine) as well as injury to other organs. Characteristic symptoms of the disease include blood in the urine, abdominal pain and frequent urinary tract infections.

Primary hyperoxaluria type 1 is long-term debilitating and life threatening because of the high rate of kidney failure seen with the condition.

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

At the time of designation, primary hyperoxaluria type 1 affected less than 0.03 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 1,500 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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating primary hyperoxaluria type 1. Different treatments were used to prevent the accumulation of calcium oxalate such as dietary changes, high fluid intake and vitamin B.

How is this medicine expected to work?

This medicine is made up of a virus that contains the gene for producing AGXT, the enzyme that is lacking in patients with primary hyperoxaluria type 1.

When the medicine is injected into the patient, the virus is expected to carry the AGXT gene into the liver cells. These cells are then expected to produce the AGXT enzyme so that calcium oxalate is not produced in excess, and thereby helping to 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 primary hyperoxaluria type 1 had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for primary hyperoxaluria type 1 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 11 January 2012 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:

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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 substance	Indication
English	Adeno-associated viral vector of serotype 5 containing the human alanine-glyoxylate aminotransferase gene	Treatment of primary hyperoxaluria type 1
Bulgarian	Адено-свързан вирусен вектор от серотип 5, съдържащ човешки ген на аланин-глиоксилат аминотрансфераза.	Лечение на първична хипероксалурия тип 1
Czech	Adeno-asociovaný virový vektor sérotypu 5 obsahující gen pro lidskou alaninglyoxylátaminotransferázu.	Léčba primární hyperoxalurie typu 1
Danish	Adeno-associeret viral vektor af serotype 5 indeholdende det humane alanin-glyoxylat aminotransferase-gen.	Behandling af primær hyperoxaluri type 1
Dutch	Adenogeassocieerde virale vector van serotype 5 welke het gen voor humaan alanine-glyoxylaataminotransferase bevat.	Behandeling van primaire hyperoxalurie type 1
Estonian	5. serotüübi adeno-assotsieerunud viiruse vektor, mis sisaldab inimese alaniini-glüoksülaadi aminotransferaasi geeni.	1. tüüpi esmase hüperoksaluuria ravi
Finnish	Serotyypin 5 AAV-vektori, joka sisältää ihmisen alaniiniglyoksylaattiaminotransferaasigeen in	Tyypin 1 primaarisen hyperoksalurian hoito
French	Vecteur viral adéno-associé de sérotype 5 contenant le gène codant pour l'alanine-glyoxylate-aminotransférase humaine.	Traitement de l'hyperoxalurie primaire de type 1
German	Ein adeno-assoziierter viraler Vektor vom Serotyp 5, der das humane Alanin-Glyoxylat-Aminotransferase-Gen enthält	Behandlung der primären Hyperoxalurie Typ 1
Greek	Ιικός φορέας σχετιζόμενος με αδενοϊό ορότυπου 5 που περιέχει το ανθρώπινο γονίδιο αμινοτρανσφεράσης αλανίνης-γλυοξυλικού.	Θεραπεία της πρωτοπαθούς υπεροξαλουρίας τύπου 1
Hungarian	5-ös szerotípusú, adeno-asszociált vírusvektor, amely a humán alanin-glioxilát-aminotranszferáz gént tartalmazza.	Az 1-es típusú, primer hiperoxaluria kezelésére
Italian	Vettore virale adeno-associato di serotipo 5 contenente il gene umano alanina-gliossilato aminotransferasi.	Trattamento delll'iperossaluria primaria di tipo 1
Latvian	5. serotipa adenoasociētā vīrusa vektors, kas satur cilvēka alanīnglioksilāta aminotransferāzes gēnu.	1. tipa primāras hiperoksalūrijas ārstēšana
Lithuanian	Adeno asocijuoto viruso vektoriaus 5 serotipas, turintis žmogaus alanino glioksilato aminotransferazės geną	Pirminės hiperoksalurijos, I tipo, gydymas

[1] At the time of designation

Language	Active substance	Indication
Maltese	Vettur ta' virus adeno assoċjat ta' serotip 5 li fih il-ġene umana alanine-glyoxylate aminotransferase.	Kura ta' iperoxalurja primarja tip 1
Polish	Wektor adenowirusowy serotypu 5, zawierający gen ludzkiej aminotransferazy alanino-glioksylanowej.	Leczenie pierwotnej hiperoksalurii typu I
Portuguese	Vetor viral adeno-associado do serotipo 5 com o gene humano da alanina-glioxilato aminotransferase.	Tratamento da hiperoxalúria primária de tipo 1
Romanian	Vector viral adeno-asociat de serotip 5, care conţine gena umană pentru alanin-glioxilat-aminotransferază.	Tratamentul hiperoxaluriei primare de tip 1
Slovak	Adeno-asociovaný vírusový vektor sérotypu 5 obsahujúci ľudský gén alanínglyoxylátovej transaminázy	Liečba primárnej hyperoxalúrie typu 1
Slovenian	Adenovirusom pridruženi virusni vektor serotipa 5, ki vsebuje človeški gen alanin-glioksilat aminotransferaze	Zdravljenje primarne hiperoksalurije vrste 1
Spanish	Vector viral adenoasociado de serotipo 5 que contiene el gen humano alanina glioxilato aminotransferasa.	Tratamiento de la hiperoxaluria primaria de tipo 1
Swedish	Adenoassocierad virusvektor av serotyp 5 innehållande den humana alaninglyoxylat-aminotransferasgenen.	Behandling av primär hyperoxaluri typ 1
Norwegian	Adenoassosiert virusvektor av serotype 5 som inneholder det humane alaninglyoksylat-aminotransferasegenet.	Behandling av primær hyperoksaluri type 1.
Icelandic	Adenó-tengd veirugenaferja af sermisgerð 5 sem felur í erfðavísi alanín-glýoxýlatamínótransferasa úr mönnum.	Meðferð við fyrsta stigs sólarhringsútskilnaði >0,49 mmól (hyperoxaluria), af gerð 1.