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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector containing porphobilinogen deaminase gene for the treatment of acute intermittent porphyria

On 29 April 2009, orphan designation (EU/3/09/632) was granted by the European Commission to Amsterdam Molecular Therapeutics BV, the Netherlands, for adeno-associated viral vector containing porphobilinogen deaminase gene for the treatment of acute intermittent porphyria.

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

What is acute intermittent porphyria?

Acute intermittent porphyria (AIP) is a genetic disease that affects the production of 'haem', a component of haemoglobin. Haemoglobin is the protein found in the red blood cells that carries oxygen around the body. Patients with AIP have attacks of abdominal (tummy) pain. They may also have symptoms affecting the nervous system, such as seizures (fits), depression, anxiety and psychosis (an altered sense of reality).

AIP is caused by abnormalities in the gene that is responsible for the production of a protein called porphobilinogen deaminase (PBGD). PBGD is involved in the production of haem by the liver. In patients with AIP, PBGD does not work properly. This causes accumulation of haem precursors (substances that are usually used to make haem) in the liver and in the blood. These substances are also found at high levels in the skin, which becomes oversensitive to light, and in the urine, which becomes red in colour.

AIP is a severe disease that is long lasting and may be life threatening because of its effects on the liver.

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

At the time of designation, AIP affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 50,000 people[*], and is below the ceiling for orphan

[*]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 504,800,000 (Eurostat 2009).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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, a medicine containing haem was authorised in some countries in the EU to treat acute attacks of AIP. In some cases, liver transplantation was used.

The sponsor has provided sufficient information to show that adeno-associated viral vector containing porphobilinogen deaminase gene might be of significant benefit for patients with AIP because it works in a different way to existing methods and could be an alternative long-term treatment for the disease. 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?

Adeno-associated viral vector containing porphobilinogen deaminase gene is a virus that contains normal copies of the PBGD gene. When injected into the liver, the virus carries the PBGD gene into the liver cells, where the gene is expected to enable the cells to start producing the PBGD protein. This will replace the defective protein, allowing the patients to start producing haem and reducing accumulation of haem precursors in the cells. This is expected to prevent attacks of AIP.

The type of virus used in this medicine ('adeno-associated virus') has been modified so that it does not cause disease in humans.

What is the stage of development of this medicine?

The effects of adeno-associated viral vector containing porphobilinogen deaminase gene have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with AIP had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for AIP or designated as 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 4 March 2009 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:

uniQure biopharma B.V.
Meibergdreef 61
1105 BA
Amsterdam
The Netherlands
Telephone: +31 20 566 7394
Telefax: +31 20 566 9272
E-mail: info@uniQure.com

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 containing porphobilinogen deaminase gene	Treatment of acute intermittent porphyria
Bulgarian	Адено-асоцииран вирусен вектор, съдържащ ген за порфобилиноген дезаминаза	Лечение на остра интермитентна порфирия
Czech	Adeno-asociovaný virový vektor obsahující gen pro porfobilinogen deaminázu	Léčba akutní intermitentní porfyrie
Danish	Adeno-associeret viral vektor, der indeholder porfobilinogen deaminase-gen	Behandling af akut intermitterende porfyri
Dutch	Adeno-geassocieerde virale vector die een porphobilinogeen deaminase gen bevat	Behandeling van acute intermittente porfyrie
Estonian	Autoloogsed hematopoeetilised tüvirakud, millele on üle kantud lentiviraalne vektor, mis kodeerib inimese beetaglobiini geeni	Ägeda vahelduva porfüüria ravi
Finnish	Porfobilinogeeni deaminaasi- geenin sisältävä adenoassosioitu virusvektori	Akuutin intermittoivan porfyrian hoito
French	Vecteur viral adéno-associé portant le gène de la porphobilinogène déaminase	Traitement de la porphyrie intermittente aiguë
German	Adeno-assoziierter viraler Vektor, der das Gen Porphobilinogen Deaminase enthaelt	Behandlung der akuten intermittierenden Porphyrie
Greek	Αδενο-συσχετιζόμενος φορέας ιού που περιέχει γονίδιο δεαμινάσης πορφοχολινογόνου	Θεραπεία οξείας ασυνεχούς πορφυρίασης
Hungarian	Porfobilinogén-deamináz gént tartalmazó adeno-asszociált vírusvektor	Akut időszakos porphyria kezelése
Italian	Vettore virale adeno-associato contenente il gene della porfobilinogeno deaminasi	Trattamento di porfiria acuta intermittente
Latvian	Ar adenovīrusu saistīts vīrusa vektors, kurš satur porfobilinogēna deaminācijas gēnu	Akūtas intermitējošas porfīrijas ārstēšana
Lithuanian	Adeno-asocijuotas virusinis vektorius, pernešantis porfobilinogendeaminazės geną	Ūminės intermituojančios eigos porfirijos gydymas
Maltese	Vettur adenovirali li fih il-ġene għal porphobilinogen deaminase	Kura tal-porfirja intermittenti akuta
Polish	Wektor wirusa sprzężonego z adenowirusem zawierającym gen deaminazy porfobilinogenu.	Leczenie ostrej przerywanej porfirii
Portuguese	Vector viral adeno-associado contendo o gene porfobilinogénio desaminase	Tratamento da porfiria intermitente aguda
Romanian	Vector viral adeno-asociat care conţine gena pentru porfobilinogen-deaminază	Tratamentul porfiriei intermitente acute

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Adenovírusový vektor obsahujúci gén porfobilinogén-deamináza	Liečba akútnej intermitentnej porfýrie
Slovenian	Adenovirusom pridruženi virusni vektor, ki vsebuje gen porfobilinogendeaminaze	Zdravljenje akutne intermitentne porfirije
Spanish	Vector vírico adenoasociado que contiene el gen de la porfobilinogeno deaminasa	Tratamiento de la porfiria aguda intermitente
Swedish	Adeno associerad viral vektor innehållande genen för porphobilinogen deaminase	Behandling av akut intermittent porfyri
Norwegian	Adeno-assosiert viral vektor som inneholder genet for porfobilinogen deaminase	Behandling av akutt intermitterende porfyri
Icelandic	AAV-ferja (adeno-associated viral vector) sem inniheldur porfóbilínógen deamínasa erfðavísi	Meðferð við bráðum porfýríuköstum með hléum á milli