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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 8 containing the human *UGT1A1* gene for the treatment of Crigler-Najjar syndrome

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Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 22 August 2014, orphan designation (EU/3/14/1321) was granted by the European Commission to Fondazione Telethon, Italy, for adeno-associated viral vector serotype 8 containing the human *UGT1A1* gene for the treatment of Crigler-Najjar syndrome.

What is Crigler-Najjar syndrome?

Crigler-Najjar syndrome is a genetic disorder in which there is an accumulation of high amounts of toxic bilirubin in the body.

Bilirubin is a waste product that results from the breakdown of haemoglobin from old or damaged red blood cells. Normally bilirubin is converted in the liver to a less toxic, soluble form called 'conjugated' bilirubin that can be excreted into the bile and so removed from the body via the gut. However, patients with this condition lack the enzyme required to convert the bilirubin and as a result it accumulates in the liver and then in the blood stream and body tissues, where it can lead to damage.

Because of the yellow colour of bilirubin, jaundice, which is the yellowing of the skin and eyes, is usually seen within a few days of birth. The most severe complication is kernicterus, where bilirubin causes damage to the brain tissue that can lead to serious problems with muscle tone, movement, hearing and intellectual ability.

The condition is long-term debilitating and life threatening due to the development of kernicterus.



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

At the time of designation, Crigler-Najjar syndrome affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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, there was no satisfactory method of treatment authorised in the EU for patients with Crigler-Najjar syndrome. Some patients were given treatments such as phototherapy (using light of certain wavelengths to break down some of the bilirubin), blood transfusions and liver transplantation.

How is this medicine expected to work?

Crigler-Najjar syndrome is caused by mutations (defects) in a gene called *UGT1A1*, which is needed for the body to produce the enzyme that converts unconjugated bilirubin into the conjugated form that can be easily removed from the body. This medicine is made of a virus that contains a normal copy of the *UGT1A1* gene. When given to the patient the virus is expected to carry the gene into the cells of the liver, enabling the cells to produce the required enzyme, thus reducing levels of bilirubin in the body and preventing development of symptoms.

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 Crigler-Najjar syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Crigler-Najjar syndrome 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 10 July 2014 recommending the granting of this designation.

*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. At the time of designation, this represented a population of 512,900,000 (Eurostat 2014).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Adeno-associated viral vector serotype 8 containing the human <i>UGT1A1</i> gene	Treatment of Crigler-Najjar syndrome
Bulgarian	аденосвързан вирусен вектор серотип 8, съдържащ човешки <i>UGT1A1</i> ген	Лечение на синдром на Crigler-Najjar
Croatian	Adeno-povezani virusni vektor serotipa 8 koji sadrži ljudski gen <i>UGT1A1</i>	Liječenje Crigler-Najjarovog sindroma
Czech	Sérotyp 8 adeno asociovaný virový vektor, obsahující lidský gen <i>UGT1A1</i>	Léčba Crigler-Najjarova syndromu
Danish	Adenoassocieret viral vektor serotype 8 indeholdende det humane <i>UGT1A1</i> gen	Behandling af Crigler-Najjar syndrom
Dutch	Adenogeassocieerde virale vector, serotype 8, welke het humane gen <i>UGT1A1</i> bevat	Behandeling van Crigler-Najjar syndroom
Estonian	Adenoga assotsieeruv viirusvektori serotüüp 8, mis sisaldab inimese <i>UGT1A1</i> geeni	Crigler-Najjar'i sündroomi ravi
Finnish	Adenoassosioitu virusvektori, serotyyppiä 8, joka sisältää ihmisen <i>UGT1A1</i> geenin	Crigler-Najjar syndrooman hoito
French	Vecteur viral adéno-associé de sérotype 8 contenant le gène humain <i>UGT1A1</i>	Traitement du syndrome de Crigler-Najjar
German	Das humane <i>UGT1A1</i> Gen beinhaltender, adeno-assoziiertes viraler Vektor Serotyp 8	Behandlung des Crigler-Najjar Syndroms
Greek	Αδενο-σχετιζόμενος ιικός φορέας ορότυπου 8 που περιέχει το ανθρώπινο γονίδιο <i>UGT1A1</i>	Θεραπεία του συνδρόμου Crigler-Najjar
Hungarian	Humán <i>UGT1A1</i> gént tartalmazó 8-as szerotípusú adeno-asszociált vírus vektor	Crigler-Najjar szindróma kezelése
Italian	Vettore virale adeno-associato del serotipo 8 contenente il gene umano <i>UGT1A1</i>	Trattamento della sindrome di Crigler-Najjar
Latvian	Adeno-saistītā virālā vektora 8. serotips, kas satur cilvēka <i>UGT1A1</i> gēnu	Krīglera un Nadžāra sindroma ārstēšana
Lithuanian	Adeno-asocijuotas viruso vektoriaus 8 serotipas, pernešantis žmogaus <i>UGT1A1</i> geną	Crigler Nadjjar'o sindromo gydymas
Maltese	Vettur imnissel mill-adenovirus tas-serotip 8 li fih il-gene uman <i>UGT1A1</i>	Kura tas-sindrome ta' Crigler Najjar
Polish	Wektor adenowirusowy serotypu 8 zawierający ludzki gen <i>UGT1A1</i>	Leczenie zespołu Criglera-Najjara
Portuguese	Vector viral adeno-associado de serotipo 8 contendo o gene humano <i>UGT1A1</i>	Tratamento de síndrome de Crigler-Najjar
Romanian	Vector viral adeno-asociat de serotip 8 conținând gena umană <i>UGT1A1</i>	Tratamentul sindromului Crigler Najjar
Slovak	Adeno-asociovaný vírusový vektor sérotypu 8 obsahujúci ľudský gén <i>UGT1A1</i>	Liečba Criglerovho-Najjarovho syndrómu

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Adeno-pridruženi virusni vektor serotipa 8, ki vsebuje človeški gen <i>UGT1A1</i>	Zdravljenje sindroma Crigler-Najjar
Spanish	Vector viral adenoasociado del serotipo 8 que contiene el gene humano <i>UGT1A1</i>	Tratamiento del síndrome de Crigler-Najjar
Swedish	Adenoassocierad virusvektor serotyp 8, innehållande den mänskliga genen <i>UGT1A1</i>	Behandling av Crigler-Najjar syndrom
Norwegian	Adenoassosiert virusvektor serotype 8 som inneholder det humane genet <i>UGT1A1</i>	Behandling av Crigler Najjar syndrom
Icelandic	Adenótengd veirufurja af sermisgerð 8 sem inniheldur manna <i>UGT1A1</i> gen	Meðfrð við Crigler-Najjar heilkenni