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Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector containing a codon-optimized Padua derivative of human coagulation factor IX cDNA for the treatment of haemophilia B

On 21 March 2018, orphan designation (EU/3/18/1999) was granted by the European Commission to uniQure biopharma B.V., the Netherlands, for recombinant adeno-associated viral vector containing a codon-optimized Padua derivative of human coagulation factor IX cDNA (also known as AMT-061) for the treatment of haemophilia B.

What is haemophilia B?

Haemophilia B is an inherited bleeding disorder caused by the lack of factor IX, a protein involved in the blood coagulation (clotting) process. Patients with haemophilia B are more prone to bleeding than normal and have poor wound healing after injury or surgery. Internal bleeding can also happen within muscles or in the joints, such as the elbows, knees and ankles. This can lead to permanent damage if it happens repeatedly.

Haemophilia B is a debilitating disease that is life long and may be life threatening because bleeding can also happen in the brain and spinal cord, the throat or the gut.

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

At the time of designation, haemophilia B affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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, medicines containing factor IX were authorised in the EU for the treatment of haemophilia B, to replace the missing protein. However, factor IX medicines did not work in some patients with haemophilia B because the immune system (the body's natural defences) can produce

[*]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 517,400,000 (Eurostat 2018).

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'inhibitors' (antibodies) against factor IX which stop the factor IX medicine from working. In these cases, other treatments needed to be used, such as factor VIIa (the activated form of factor VII, another protein involved in blood clotting), either alone or as part of a combination treatment.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with haemophilia B because laboratory studies show that it can increase the amount of factor IX circulating in the blood. The way the medicine works means that patients may not need or may need less frequent treatment with factor IX medicines. 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?

In patients with haemophilia B, the gene for producing factor IX is defective, which stops them making factor IX.

This medicine is made of a virus that contains normal copies of the gene responsible for producing factor IX. When injected into the patient's vein, it is expected that the virus will be carried to the liver where the gene will be taken up into the patient's liver cells and start producing factor IX. It is expected that a single dose of the medicine will maintain raised levels of factor IX for a long time thereby reducing bleeding.

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 haemophilia B had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for haemophilia B 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 15 February 2018 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	Recombinant adeno-associated viral vector containing a codon-optimized Padua derivative of human coagulation factor IX cDNA	Treatment of haemophilia B
Bulgarian	Рекомбинантен адено-свързан вирусен вектор, съдържащ кодон-оптимизирано Падуа производно на кДНК на човешки коагулационен фактор IX	Лечение на хемофилия B
Croatian	Rekombinantni adeno-povezani virusni vektor koji sadrži kodon-optimiziranu cDNK Padova derivata ljudskog faktora zgrušavanja IX	Liječenje hemofilije B
Czech	Rekombinantní adeno-asociovaný virový vektor obsahující kodonově optimalizovaný padovský derivát cDNA lidského koagulačního faktoru IX	Léčba hemofilie B
Danish	Rekombinant adenoassocieret viral vektor indeholdende et kodonoptimeret Padua-derivat af human koagulationsfaktor IX-cDNA	Behandling af hæmofili B
Dutch	Recombinant-adenogeassocieerde virale vector die een codon-geoptimaliseerd Padua-derivaat van humaan bloedstollingsfactor-IX-cDNA bevat	Behandeling van hemofilie B
Estonian	Rekombinantne inimese IX hüübimisfaktori Padua derivaadi koodon-optimeeritud cDNA-d sisaldav adeno-assotsieerunud viirusvektor	Hemofiilia B ravi
Finnish	Ihmisen hyytymistekijä IX:n Padova-variantin kodonioptimoidun cDNA:n sisältävä rekombinantti-AAV-vektori	Hemofilia B:n hoito
French	Vecteur viral adéno-associé recombinant contenant un gène Padoue à codon optimisé dérivé de l'ADNc du facteur IX humain de la coagulation	Traitement de l'hémophilie B
German	Rekombinanter adeno-assoziierter viraler Vektor, der ein codon-optimiertes Padua-Derivat von humaner Gerinnungsfaktor IX cDNA enthält	Behandlung der Hämophilie B
Greek	Ανασυνδυασμένος αδενο-σχετιζόμενος ιικός φορέας που περιέχει το cDNA βελτιστοποιημένου κωδικονίου, για την παραλλαγή Πάντοβας του παράγοντα πήξης IX	Θεραπεία της αιμορροφιλίας B
Hungarian	Humán IX-es véralvadási faktor cDNS kodon-optimalizált Padua mutáns verzióját tartalmazó adeno-asszociált rekombináns vírusvektor	B típusú hemofília kezelése
Italian	Vettore virale ricombinante adeno-associato contenente il cDNA del fattore IX umano della coagulazione a codone-ottimizzato Padua-derivato	Trattamento dell'emofilia B
Latvian	Rekombinants adenoasociētā vīrusa vektors, kas satur cilvēka IX asinsreces faktora cDNA Padujas atvasinājumu ar optimizētu kodonu	B tipa hemofilijas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Rekombinantinis adeno asocijuotojo viruso vektorius, turintis kodoną, optimizuotą *Padua* derivatine žmogaus IX krešėjimo faktoriaus kDNR	Hemofilijos B gydymas
Maltese	Vettur virali rikombinanti assoċjat ma' adeno li fih derivat ta' Padua b'kodon ottimizzat ta' cDNA tal-fattur IX tal-koagulazzjoni umana	Kura ta' l-emofilja B
Polish	Rekombinowany wektor związany z adenowirusami zawierający cDNA pochodnej Padua z optymalizacją kodonów ludzkiego czynnika krzepnięcia IX	Leczenie hemofilii B
Portuguese	Vetor viral recombinante adeno-associado contendo um codão Pádua otimizado derivado do ADNc do fator IX da coagulação humana	Tratamento da hemofilia B
Romanian	Vector viral adeno-asociat recombinant conținând un codon optimizat al ADNc al factorului IX de coagulare uman Padua derivat	Tratamentul hemofiliei B
Slovak	Rekombinantný adeno-asociovaný vírusový vektor obsahujúci kodónovo optimalizovaný padovský derivát ľudského koagulačného faktora IX cDNA	Liečba hemofílie B
Slovenian	Rekombinantni adenovirusom pridruženi vektor, ki vsebuje kodonsko optimirani padovanski derivat cDNA humanega koagulacijskega faktorja IX	Zdravljenje hemofilije B
Spanish	Vector adenovírico recombinado que contiene cDNA del factor de la coagulación IX Padua, con un codón optimizado	Tratamiento de la hemofilia B
Swedish	Rekombinant adenoassocierad virusvektor innehållande ett kodonoptimerat Padua-derivat av human koagulationsfaktor IX cDNA	Behandling av hemofili B
Norwegian	Rekombinant adenoassosiert virusvektor som innholder et kodonoptimalisert Padua-derivat av human koagulasjonsfaktor IX cDNA	Behandling av hemofili B
Icelandic	Raðbrigða adenó-tengd veiruferja sem inniheldur tákn-bætta manna Padua-afleiðu storkuþáttar IX cDNA	Meðferð við dreyrasýki B