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Public summary of opinion on orphan designation

Protein-based delivery vector carrying a DNA payload encoding an RNA-guided nuclease that targets stx genes of Shiga toxin-producing *Escherichia coli* for the prevention of haemolytic uraemic syndrome

On 21 August 2020, orphan designation EU/3/20/2316 was granted by the European Commission to Eligo Bioscience, France, for protein-based delivery vector carrying a DNA payload encoding an RNA-guided nuclease that targets stx genes of Shiga toxin-producing *Escherichia coli* for the prevention of haemolytic uraemic syndrome.

What is haemolytic uraemic syndrome?

Haemolytic uraemic syndrome (HUS) is a disorder characterised by three main signs: haemolysis (destruction of red blood cells), thrombocytopenia (a decrease in the number of platelets, components that help the blood to clot) and kidney failure. HUS can lead to formation of blood clots that damage small vessels supplying the organs and may cause problems in the brain and nervous system, and damage to other organs such as the heart, gut and kidneys.

HUS is often associated with infections with *Escherichia coli* bacteria that produce a toxin called Shiga toxin (Shiga toxin-producing *E. coli* or STEC). The toxin damages the lining of blood vessels, triggering the symptoms of the disease. STEC-associated HUS primarily affects young children who catch the infection mostly through contaminated food sources.

HUS is a long-lasting and life-threatening disease mainly because of the risk of kidney failure and complications affecting the brain and other organs.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of developing HUS was estimated to be approximately 0.24 in 10,000 people in the European Union (EU). This was equivalent to a total of around 12,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000.

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).



This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of prevention are available?

At the time of designation, no satisfactory methods of prevention for HUS were authorised in the EU. The medicine Soliris was authorised to treat patients affected by non-infectious forms of the condition (atypical HUS), while patients who developed STEC-related HUS were managed with supportive treatment. Transfusions of red blood cells and platelets were given as needed, as well as medicines to manage complications such as seizures (fits). Dialysis (a blood clearance technique) was used if the disease progressed to kidney failure. Some patients needed a kidney transplant.

How is this medicine expected to work?

This medicine contains genetic material (DNA) which, once in the cells, leads to the production of an enzyme that will target and eliminate the *Escherichia coli* that produce the Shiga toxin causing the symptoms of the disease. By eliminating the bacteria, the medicine is expected to reduce the production of the toxin and thereby prevent HUS.

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 this medicine in experimental models was ongoing.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the prevention of HUS or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 2020, 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

Contact details of the current sponsor for this orphan designation can be found on [EMA website](#).

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	Protein-based delivery vector carrying a DNA payload encoding an RNA-guided nuclease that targets <i>stx</i> genes of Shiga toxin-producing <i>Escherichia coli</i>	Prevention of haemolytic uraemic syndrome
Bulgarian	Протеинов вектор носещ ДНК, кодираща РНК-управлявана нуклеаза, насочена към <i>stx</i> гените на <i>Escherichia coli</i> продуцираща шига токсин	Превенция на хемолитично-уремичен синдром
Croatian	Vektor isporuke temeljen na proteinu koji nosi DNA korisnog opterećenja koji kodira RNA vođenu nukleazu koja cilja <i>stx</i> gene Shiga toksina kojeg proizvodi <i>Escherichia coli</i>	Prevenција hemolitičnog uremijskog sindroma
Czech	Doručovací vektor na bázi proteinu nesoucí DNA kódující RNA-řízenou nukleázu, která cílí na <i>stx</i> geny <i>Escherichia coli</i> produkující Shiga toxin	Prevence hemolyticko-uremického syndromu
Danish	Proteinbaseret leveringsvektor, der bærer en DNA region kodende for en RNA-styret nuclease målrettet mod <i>stx</i> -gener fra Shiga-toksinproducerende <i>Escherichia coli</i>	Forebyggelse af hæmolytisk uræmisk syndrom
Dutch	Eiwit-gebaseerde leveringsvector welke een DNA ladingslast draagt, coderend voor een RNA-gestuurde nuclease gericht op <i>stx</i> genen van Shiga toxine-producerende <i>Escherichia coli</i>	Preventie van hemolytisch uremisch syndroom
Estonian	Shiga-toksiini tootva <i>Escherichia coli stx</i> geenide vastu suunatud RNA-juhitud nukleaasi kodeerivat DNAd kandev kullervalk	Hemolüütilis-ureemilise sündroomi ennetamine
Finnish	Proteiinipohjainen kuljetusvektori, joka kantaa DNAta, joka koodaa RNA-ohjattua nukleasia, joka kohdistuu Shiga-toksiinia tuottavan <i>Escherichia coli</i> <i>stx</i> -geeneihin	Hemolyyttis-ureemisen oireyhtymän ennaltaehkäisy
French	Vecteur de transduction à base de protéines portant une charge d'ADN codant pour une nucléase guidée par de l'ARN ciblant les gènes <i>stx</i> d' <i>Escherichia coli</i> produisant la toxine Shiga	Prevention du syndrome hémolytique et urémique
German	Proteinbasierter Vektor, der eine DNA-Nutzlast trägt, die eine RNA-gesteuerte Nuklease kodiert, die auf <i>stx</i> -Gene von Shiga-Toxin-produzierenden <i>Escherichia coli</i> abzielt	Prävention des hämolytisch-urämischen Syndroms
Greek	Πρωτεϊνικός φορέας που μεταφέρει ένα φορτίο DNA που κωδικοποιεί μια RNA-καθοδηγούμενη νουκλεάση που στοχεύει τα <i>stx</i> γονίδια της <i>Escherichia coli</i> που παράγει Shiga-τοξίνη	Πρόληψη του αιμολυτικού ουραιμικού συνδρόμου

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	Proteinbasiertor vektor, der eine DNA-Nutzlast trägt, die eine RNA-gesteuerte Nuklease kodiert, die auf <i>stx</i> -Gene von Shiga-Toxin-produzierenden <i>Escherichia coli</i> abzielt	Hemolitikus urémiás szindróma megelőzésére
Italian	Vettore di trasduzione proteico portante un carico di DNA che codifica per una nucleasi guidata dall'RN che ha come target i geni <i>stx</i> dell' <i>Escherichia coli</i> producent Shiga-toxin	Prevenzione della síndrome emolitico-uremica
Latvian	Proteīnu-bāzes pārneses vektors, kas pārnes lietderīgo DNS, kas kodē RNS-vadītu nukleāzi, kas vērsta pret Šinga toksīnu veidojošu <i>Escherichia coli stx</i> gēniem	Hemolītiski urēmiskā sindroma prevencija
Lithuanian	Baltymų pagrindo pristatymo vektorius, nešantis DNR, koduojančią RNR-vedamą nukleazę, nukreiptą prieš Shiga toksiną gaminančios <i>Escherichia</i>	Hemolizinio ureminio sindromo prevencijai
Maltese	Vettur ta' twassil ibbażat fuq il-proteina li jgħorr tagħbija tad-DNA li tikkodifika nukleazi gwidata mill-RNA li jkollha fil-mira ġeni <i>stx</i> ta' <i>Escherichia coli</i> li tipproduci t-tossina Shiga	Prevenzjoni tas-sindrome uraemiku emolitiku
Polish	Białkowy wektor będący nośnikiem ładunku DNA kodującego nukleazę sterowaną RNA, nakierowaną na geny <i>stx Escherichia coli</i> wytwarzającej toksynę Shiga	Zapobieganie zespołowi hemolityczno-mocznicowemu
Portuguese	Elementos capsídicos de transporte de um DNA que codifica uma nuclease guiada por RNA que tem como alvo os genes <i>stx</i> da toxina Shiga produzida por <i>Escherichia coli</i>	Prevenção da síndrome hemolítica urémica
Romanian	Vector de transductie proteic purtător al unei încărcături de ADN care codifică o nuclează ARN ghidată care vizează genele <i>stx Escherichia coli</i> care produce toxina Shiga	Prevenția sindromului hemolitic uremic
Slovak	Proteínovo založený vektor nesúci DNA, kódujúci RNA navigovanú nukleázu, ktorá zamierava <i>stx</i> gény <i>Escherichia coli</i> produkujúce Shiga toxín.	Hemolyticko-uremický syndróm
Slovenian	Proteinski dostavni vektor, ki nosi DNK, kodirano za RNK vodeno nukleazo, usmerjeno proti <i>stx</i> genom <i>Escherichie coli</i> , ki proizvaja šiga toksin	Preprečevanje hemolitičnega uremičnega sindroma
Spanish	Vector entregante a base de proteínas que transporta una carga de ADN que codifica una nucleasa dirigida por ARN que objectiva los genes <i>stx</i> de <i>Escherichia coli</i> que producen la toxina Shiga	Prevenzion del síndrome urémico hemolítico
Swedish	Proteinbaserad vector bärande på DNA som kodar för ett RNA-guidat nukleas riktat mot <i>stx</i> gener hos Shigatoxinproducerande <i>Escherichia coli</i>	Förebyggande av hemolytiskt uremiskt syndrom

Language	Active ingredient	Indication
Norwegian	Proteinbasert vektorleverandør som bærer en DNA-payload som koder for en RNA-guided nuklease rettet mot <i>stx</i> -genene av Shigatoksin-produserende <i>Escherichia coli</i>	Forebygging av hemolytisk-uremisk syndrom
Icelandic	Próteinferja sem ber DNA-farm sem kóðar fyrir RNA-stýrðum nukleasa sem ræðst á <i>stx</i> -gen <i>Escheria coli</i> bakteríunnar sem framleiðir Shiga-eitur	Forvörn gegn blóðlýsuþvageitrunarheilkenni