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Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 3B encoding human multidrug resistance protein 3A for the treatment of progressive familial intrahepatic cholestasis

On 22 April 2020, orphan designation EU/3/20/2267 was granted by the European Commission to Vivet Therapeutics S.A.S., France, for adeno-associated viral vector serotype 3B encoding human multidrug resistance protein 3A (also known as VTX-803) for the treatment of progressive familial intrahepatic cholestasis.

What is progressive familial intrahepatic cholestasis?

Progressive familial intrahepatic cholestasis is an inherited condition that causes progressive liver disease, which normally leads to liver failure. In progressive familial intrahepatic cholestasis, bile acids, essential components of bile (a fluid produced by the liver which helps digestion), build up in liver cells, becoming toxic to the liver and causing cirrhosis (scarring). Symptoms usually begin in infancy and include severe itching, jaundice (yellowing of the skin and eyes), delayed growth, pancreatitis (inflammation of the pancreas) and bleeding inside the stomach or the gut. At later stages, high blood pressure in the vein that supplies blood to the liver and liver failure will occur.

Progressive familial intrahepatic cholestasis is a long-term debilitating and life-threatening condition because, when the disease progresses, it may lead to liver cirrhosis and liver failure, and may increase the risk of liver cancer. Patients often need liver transplantation.

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

At the time of designation, progressive familial intrahepatic cholestasis 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).

*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).

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What treatments are available?

At the time of designation, ursodeoxycholic acid (UDCA) was authorised in France for a type of the condition called progressive familial intrahepatic cholestasis type III. Several medicines, including UDCA, were also used in the EU to treat the itching.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with progressive familial intrahepatic cholestasis because early laboratory data indicated that the medicine could improve liver function in the long term, potentially avoiding the need for continuous daily treatment. 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?

Progressive familial intrahepatic cholestasis type III is caused by mutations (changes) in the gene for a protein known as multidrug resistance protein 3 (MDR3). MDR3 helps to transport certain lipids that inactivate bile acids and help to protect liver cells from toxic substances in the bile fluid. Because of the mutations, MDR3 does not work properly and toxic bile acids build up in liver cells. This medicine is made of a virus that contains a normal copy of the gene for MDR3. When given to the patient, the virus is expected to carry the gene into the cells of the liver, enabling the cells to produce working MDR3, thus reducing build-up of toxic bile acids and preventing development of symptoms.

The 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 had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of progressive familial intrahepatic cholestasis 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 19 March 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

Sponsor's contact details:

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Adeno-associated viral vector serotype 3B encoding human multidrug resistance protein 3A	Treatment of progressive familial intrahepatic cholestasis
Bulgarian	Аденоасоцииран вирусен вектор серотип 3B, кодиращ протеин 3A на човешката множествена лекарствена резистентност	Лечение на прогресивна фамилна интрахепатална холестаза
Croatian	Adeno-asocirani virusni vektor serotipa 3B, koji kodira za humani protein otpornosti na više lijekova 3A	Liječenje progresivne obiteljske intrahepatične kolestaze
Czech	Adeno-asociovaný virový vektor sérotypu 3B kódující lidskou proteinu mnohočetné lékové rezistence 3A	Léčba progresivní familiární intrahepatální cholestázy
Danish	Adeno-associeret virus serotype 3B vektor, som koder for human multilægemiddelresistens protein 3A	Behandling af progressiv familiær intrahepatisk kolestase
Dutch	Adeno-geassocieerd virus serotype 3B vector die codeert voor humane multidrug resistentie eiwit 3A	Behandeling van progressieve familiale intrahepatische cholestase
Estonian	Adeno-assotsieerunud viirusvektor serotüüp 3B, mis kodeerib inimese multiravimresistentsusevalku 3A	Progresseeruva perekondliku intrahepaatilise kolestaasi ravi
Finnish	Adenoassosioitu virusvektori, serotyyppi 3B, joka koodaa ihmisen monilääkeresistenssiproteiini 3A:ta	Etenevän familiaalisen intrahepaattisen kolestaasin hoito
French	Vecteur viral adéno-associé de sérotype 3B codant la protéine humaine de multirésistance aux médicaments 3A	Traitement de la cholestase intrahépatique familiale progressive
German	Adeno-assoziierter Viraler Vektor vom Serotyp 3B, der für das humane Multidrug-Resistenz-Protein-3A codiert	Behandlung progressiver familiärer intrahepatischer Cholestase
Greek	Αδενο-σχετιζόμενος ιικός φορέας οροτύπου 3B που κωδικοποιεί την ανθρώπινη πρωτεΐνη πολυφαρμακευτικής αντοχής 3A	Θεραπεία της προοδευτικής οικογενούς ενδοηπατικής χολόστασης
Hungarian	Humán multidrog rezisztencia 3A fehérjét kódoló, 3B szerotípusú adeno-asszociált virális vektor	Progresszív familiáris intrahepaticus cholestasis kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Vettore virale adeno-associato di sierotipo 3B che codifica per proteina di resistenza multifarmaco 3A umana	Trattamento della Colestasi progressiva familiare intraepatica
Latvian	Adeno-asociētā vīrusa serotipa 3B vektors, kas kodē cilvēka vairāku zāļu rezistences proteīnu 3A	Progresīvās ģimenes intrahepatiskās holestāzes ārstēšana
Lithuanian	Adenoasocijuoto viruso vektoriaus 3B serotipas, koduojantis žmogaus daugeliui vaistų atsparus 3A baltymas	Progresuojančios šeiminės intrahepatinės cholestazės gydymas
Maltese	Vettur virali assoċjat mal-adeno tas-serotip 3B li jikkodifika l-proteina umana ta' reżistenza għal ħafna mediċini 3A	Kura tal-kolestasi intra-epatika li tintiret progressiva
Polish	Wektor wirusowy związany zadenowirusami serotypu 3B, kodujący ludzkie białko oporności wielolekowej 3A	Leczenie postępującej rodzinnej cholestazy wewnątrzwątrobowej
Portuguese	Vector viral adeno-associado de serotipo 3B que codifica a proteína humana de multirresistência a fármacos 3A	Tratamento da colestase intra-hepática familiar progressiva
Romanian	Vector viral adeno-asociat de serotip 3B, care codifică proteina rezistenţei multi-drog 3A umană	Tratamentul colestazei intrahepatice familiale progresive
Slovak	Adeno-asociovaný vírusový vektor sérotypu 3B kódujúci ľudský protein pre rezistenciu na lieky	Liečba progresívnej familiárnej intrahepatálnej cholestázy
Slovenian	Adenoasociiran virusni vektor serotipa 3B, ki kodira človeški protein 3A za odpornost na več zdravil	Zdravljenje progresivne familiarne intrahepatične holestaze
Spanish	Vector viral adenoasociado del serotipo 3B que codifica la proteína de resistencia a multifármacos 3A humana	Tratamiento de la colestasis intrahepática familiar progresiva
Swedish	Adenoassocierad virusvektor serotyp 3B som kodar för humant multiläkemedelsresistent protein3A	Behandling av progressiv familjär intrahepatisk kolestas
Norwegian	Adenoassosiert virusvektor serotype 3B som koder for humant multilegemiddelresistent protein 3A	Behandling av progressiv familiær intrahepatisk kolestase
Icelandic	Adenótengd veirugenaferja af sermisgerð 3B sem kóðar fyrir fjöllyfja ónæmispróteini 3A	Meðferð á ágengri ættgengri innanlifrar gallteppu