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Public summary of opinion on orphan designation

Recombinant adeno-associated viral vector serotype S3 containing codon-optimised expression cassette encoding human coagulation factor IX variant for the treatment of haemophilia B

On 26 October 2018, orphan designation (EU/3/18/2080) was granted by the European Commission to Freeline Therapeutics Ltd, United Kingdom, for recombinant adeno-associated viral vector serotype S3 containing codon-optimised expression cassette encoding human coagulation factor IX variant (also known as FLT180a) 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 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 16,000 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 preliminary data 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?

Patients with haemophilia B cannot make enough working factor IX because the gene for producing the clotting factor is damaged.

This medicine is made of a virus that contains copies of the gene responsible for producing factor IX. When injected into the patient, it is expected that the virus will be carried into the 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?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial with the medicine in patients with haemophilia B was ongoing.

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 13 September 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 serotype S3 containing codon-optimised expression cassette encoding human coagulation factor IX variant	Treatment of haemophilia B
Bulgarian	Рекомбинантен адено-асоцииран вирусен вектор, серотип S3, съдържащ кодон-оптимизирана експресионна касета, кодираща човешки коагулационен фактор IX вариант	Лечение на хемофилия B
Croatian	Rekombinantni adeno-povezani virusni vektor serotipa S3 koji sadrži kodon-optimiziranu ekspresijsku kasetu koja kodira varijantu faktora humanog koagulacijskog faktora IX	Liječenje hemofilije B
Czech	Rekombinantní adeno-asociovaný virový vektor sérotypu S3 obsahující expresní kazetu optimalizovanou kodonem kódující variantu lidského koagulačního faktoru IX	Léčba hemofilie B
Danish	Rekombinant adenoassocieret viral vektor serotype S3 indeholdende en kodonoptimeret ekspressionskassette kodende for human koagulationsfaktor IX-variant	Behandling af hæmofili B
Dutch	Recombinant adeno-geassocieerde virale vector serotype S3 welke codon-geoptimiseerd expressie-cassette bevat welke codeert voor humane coagulatiefactor IX variant	Behandeling van hemofilie B
Estonian	Rekombinantne adeno-assotsieerunud viirusvektori serotüüp S3, mis sisaldab inimese IX hüübimisfaktori varianti kodeerivat koodon-optimeeritud ekspressioonikassetti	Hemofiilia B ravi
Finnish	Rekombinantti adenoassosioitu virusvektori S3, jonka sisältämä kodonioptimoitu ekspressiokasetti koodaa ihmisen hyytymistekijä IX:n varianttia	Hemofilia B:n hoito
French	Vecteur viral adeno-associe recombinant de serotype S3 contenant une cassette a expression codon-optimise qui codifie la variante de facteur de coagulation IX humain	Traitement de l'hémophilie B
German	Rekombinanter adeno-assoziiertes-Virus-Vektor Serotyp S3 umfassend eine Codon-optimierte Expressionskassette, die eine Variante des menschlichen Koagulationsfaktors IX kodiert	Behandlung der Hämophilie B
Greek	Ανασυνδυσμένος αδενο-σχετιζόμενος ιικός φορέας οροτύπου S3 που περιέχει μία κασέττα έκφρασης βελτιστοποιημένων κωδικονίων που κωδικοποιεί μία παραλλαγή του ανθρώπινου παράγοντα πήξης IX	Θεραπεία της αιμορροφιλίας B

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	Humán koagulációs factor IX változatát kódoló kodon-optimalizált expressziós kazettát tartalmazó S3 szerotípusú rekombináns adeno-asszociált vírusvektor	B típusú hemofília kezelése
Italian	Vettore virale adeno-associaio recombinante di serotipo S3 contenente una cassetta di espressione con codon ottimizzato che codifica una variante del fattore IX della coagulazione umana	Trattamento dell'emofilia B
Latvian	Rekombinants adeno-asociētā virālā vektora S3 serotips, kas satur ekspresijas kaseti ar optimizētu kodonu, kas kodē cilvēka koagulācijas faktora IX variantu	B tipa hemofilijas ārstēšana
Lithuanian	Rekombinantinis su adeno virusu susijęs vektoriaus serotipas S3, turintis kodono raišką optimizuojančią kasetę, koduojančią žmogaus krešėjimo IX faktoriaus variantą	Hemofilijos B gydymas
Maltese	Vettur virali adeno-assoċjat tas-serotip S3 rekombinanti li fih każett ta' espressjoni tal-codon li jkun ottimizzat biex jagħti spinta lill-espressjoni li tagħti l-kodiċi għall-varjant tal-fattur IX tal-koagulazzjoni umana	Kura ta' l-emofilja B
Polish	Rekombinowany związany z adenowirusami wektor wirusowy serotypu S3 zawierający kasetę ekspresyjną ze zoptymalizowanymi kodonami, kodującą wariant ludzkiego czynnika krzepnięcia IX	Leczenie hemofilii B
Portuguese	Vetor viral adeno-associado recombinante de sorotipo S3, contendo uma cassete de expressão com codão otimizado que codifica a variante do fator IX da coagulação humana	Tratamento da hemofilia B
Romanian	Vector viral recombinant adeno-asociat de serotip S3 ce conţine caseta de expresie codon-optimizată ce codifică o variant factorului uman de coagulare IX	Tratamentul hemofiliei B
Slovak	Rekombinantný adeno-asociovaný vírusový vektor sérotypu S3 obsahujúci kodón-optimalizovanú exprimujúcu kazetu kódujúcu viariant IX ľudského koagulačného faktora	Liečba hemofílie B
Slovenian	Rekombinantni adeno-povezani virusni vektor serotipa S3 vsebujoč s kodo optimizirano ekspresijsko kaseto, ki kodira za varianto človeškega koagulacijskega faktorja IX	Zdravljenje hemofilije B
Spanish	Vector viral adenoasociado recombinanted de serotipo S3 que contiene un casete con un codon optimizado que codifica del factor de coagulacion variante humano IX	Tratamiento de la hemofilia B
Swedish	Rekombinant adeno-associerad virusvektor serotyp S3 innehållande en kodonoptimiserad utryckskassett so kodar för human koagulationsfaktor IX variant	Behandling av hemofili B

Language	Active ingredient	Indication
Norwegian	Rekombinant adenoassosiert virusvektor serotype S3 som inneholder en kodonoptimalisert ekspresjonskassett som koder for en human variant av koagulasjonsfaktor IX	Behandling av hemofili B
Icelandic	Raðbrigða adenoveirutengd genaferja af sermisgerð S3 sem inniheldur tjáningarstæðu af tákni sem hefur verið magnað og kóðar fyrir afbrigði manna storkuþáttar IX	Meðferð við dreyrasýki B