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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adeno-associated viral vector serotype 5 containing a B-domain deleted variant of human coagulation factor VIII gene for the treatment of haemophilia A

On 21 March 2016, orphan designation (EU/3/16/1622) was granted by the European Commission to BioMarin Europe Ltd., United Kingdom, for adeno-associated viral vector serotype 5 containing a B-domain deleted variant of human coagulation factor VIII gene (also called BMN 270) for the treatment of haemophilia A.

What is haemophilia A?

Haemophilia A is an inherited bleeding disorder that is caused by the lack of factor VIII, which is one of the proteins involved in the blood coagulation (clotting) process. Patients with haemophilia A are more prone to bleeding than normal and have prolonged bleeding after injury or surgery. Bleeding can also happen within muscles or the spaces in the joints, such as the elbows, knees and ankles. This can lead to permanent injury if it happens repeatedly.

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

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

At the time of designation, haemophilia A affected approximately 0.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 36,000 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 VIII were authorised in the EU for the treatment of haemophilia A, to replace the missing protein. However, not all patients with

*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 513,700,000 (Eurostat 2016).



haemophilia A could benefit from these medicines because the immune system (the body's natural defences) can produce 'inhibitors' (antibodies) against factor VIII and thereby stop the factor VIII 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 this medicine might be of significant benefit for patients with haemophilia A because results from laboratory studies show that a single administration can result in sustained production of factor VIII and restore factor VIII activity. 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?

This medicine is made of a virus that has been modified to contain the gene for factor VIII, which is lacking in patients with haemophilia A. After being given once to the patient as an injection into a vein, the virus is expected to carry the factor-VIII gene into the liver cells, enabling them to produce the missing factor VIII for a long period. This is expected to control the bleeding disorder.

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, clinical trials with the medicine in patients with haemophilia A were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for haemophilia A 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 18 February 2016 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, 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Adeno-associated viral vector serotype 5 containing a B-domain deleted variant of human coagulation factor VIII gene	Treatment of haemophilia A
Bulgarian	Адено-свързан вирусен вектор серотип 5, съдържащ вариант с премахнат В-домейн на гена на човешкия кръвосъсирващ фактор VIII	Лечение на хемофилия А
Croatian	Adeno-povezani virusni vektor serotipa 5 koji sadrži varijantu gena ljudskog faktora zgrušavanja VIII s izostavljenom B domenom	Liječenje hemofilije A
Czech	Adenoasociovaný virový vektor sérotyp 5 obsahující variantu genu humánního koagulačního faktoru VIII s deletovanou B doménou	Léčba hemofilie A
Danish	Adeno-associeret viral vektor serotype 5 indeholdende en B-domæne-slettet variant af humant koagulationsfaktor VIII-gen	Behandling af hæmofili A
Dutch	Adeno-geassocieerde virale vector serotype 5 die een variant van het gen voor humane stollingsfactor VIII met B-domeindeletie bevat	Behandeling van hemofilie A
Estonian	Adenoviirusega seotud viirusvektori 5. serotüüp, mis sisaldab inimese hüübimisfaktor VIII geeni B-domeeni deleteerunud varianti	Hemofiilia A ravi
Finnish	Adenoassosioitu virusvektori, serotyppi 5, joka sisältää ihmisen veren hyytymistekijä VIII:n geenivariantin, josta on poistettu B-domeeni	Hemofilia A:n hoito
French	Vecteur viral adéno-associé de sérotype 5 contenant un variant dépourvu du domaine B du gène du facteur de coagulation VIII humain	Traitemennt de l'hémophilie A
German	Adeno-assoziiertes-Virus-Vektor Serotyp 5, der eine B-Domäne-deletierte Variante des menschlichen Koagulationsfaktor-VIII-Gens enthält	Behandlung der Hämophilie A
Greek	Αδενο-σχετιζόμενος ιικός φορέας οροτύπου 5 που περιέχει μια παραλλαγή του ανθρώπινου γονιδίου του παράγοντα πηξης VIII, από τον οποίο έχει αφαιρεθεί η περιοχή B	Θεραπεία της αιμορροφιλίας A
Hungarian	Humán VIII. véralvadási faktor génjének B-domén törölt változatát tartalmazó, adeno-asszociált, 5-ös szerotípusú vírusvektor	A típusú hemofília kezelése
Italian	Vettore virale adeno-associaato di sierotipo 5 contenente una variante cancellata del dominio B del gene del Fattore VIII della coagulazione umana	Trattamento dell'emofilia A

¹ At the time of designation

Language	Active ingredient	Indication
Latvian	Adeno-asociētā vīrusa 5. serotipa vektors, kas satur cilvēka VIII asinsreces faktora gēna variantu ar B domēna delēciju	A tipa hemofilijas ārstēšana
Lithuanian	Adenoasocijuotas virusinis 5 serotipovektorius su iškirptu žmogaus VIII krešėjimo faktoriaus geno B domeno variantu	Hemofilijos A gydymas
Maltese	Vettur imnissel mill-adenovirus tas-serotip 5 li fih varjant tal-ģene tal-fattur VIII tal-koagulazzjoni uman li tneħħielu d-dominju B	Kura ta' I-emofilja A
Polish	Wektor adenowirusowy serotypu 5 zawierający wariant genu ludzkiego czynnika krzepnięcia VIII bez domeny B	Leczenie hemofilii A
Portuguese	Vetor viral adeno-associado de serotipo 5 contendo uma variante com deleção do domínio B do gene do fator VIII de coagulação humana	Tratamento da hemofilia A
Romanian	Vector viral adeno-asociat de serotip 5 conținând o variantă obținută prin deleția domeniului B a genei factorului de coagulare VIII uman	Tratamentul hemofiliei A
Slovak	Adeno-asociovaný vírusový vektorový sérotyp 5 obsahujúci variant ľudského génu koagulačného faktora VIII bez B-domény	Liečba hemofílie A
Slovenian	Adenovirusom pridruženi virusni vektor serotipa 5, ki vsebuje različico gena humanega koagulacijskega faktora VIII brez domene B	Zdravljenje hemofilije A
Spanish	Vector de adenovirus serotipo 5 que contiene una variante del gen del factor VIII de coagulación humana en el que se ha eliminado el dominio B	Tratamiento de la hemofilia A
Swedish	Adenoassocierad virusvektor serotyp 5 innehållande en β-domän-deleterad variant av genen för human koagulationsfaktor VIII	Behandling av hemofili A
Norwegian	Adeno-assosiert viral vektor serotype 5 inneholdende en B-domene-fjernet variant av human koagulasjonsfaktor VIII-gen	Behandling av hemofili A
Icelandic	Adenóltengd veiruferja af sermisgerð 5 sem inniheldur genaafbrigð með eyddu B hneppii af manna storkupþætti VIII	Meðferð við dreyrasýki A