10 July 2018
EMA/270813/2018

# Public summary of opinion on orphan designation

## Adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII for the treatment of haemophilia A

On 25 May 2018, orphan designation (EU/3/18/2015) was granted by the European Commission to Baxalta Innovations GmbH, Austria, for adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII 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 prone to bleeding and bleed for a long time after injury or surgery. Bleeding can also happen within muscles or 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 occur in the brain, spinal cord or 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, factor VIII medicines did not work in some patients with haemophilia A because the immune system (the body's natural defences)

[*]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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
**Send a question via our website** www.ema.europa.eu/contact

can produce ‘inhibitors’ (antibodies) against factor VIII which 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 the medicine might be of significant benefit for patients with haemophilia A because laboratory studies indicate that it can restore normal levels of factor VIII circulating in the blood and reduce blood loss after a single dose of the medicine. As a result, patients may not need or may need less frequent treatment with factor VIII 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 A, the gene for producing factor VIII is defective, which stops them making factor VIII.

This medicine is made of a virus that contains copies of the gene responsible for producing factor VIII. 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 VIII. It is expected that a single dose of the medicine will maintain raised levels of factor VIII 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 A was ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for haemophilia A. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 April 2018 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 languages[1], Norwegian and Icelandic

| Language | Active ingredient | Indication |
|---|---|---|
| English | Adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII | Treatment of haemophilia A |
| Bulgarian | Адено-асоцииран вирусен вектор серотип 8, съдържащ функционално копие на кодон оптимизиран F8 cDNA, кодиращ изтрит B-домейн на човешкия коагулационен фактор VIII | Лечение на хемофилия A |
| Croatian | Adeno-povezani virusni vektor serotipa 8 koji sadrži funkcionalnu kopiju F8 cDNK optimiziranu kodonom koja kodira za ljudski koagulacijski faktor VIII s izostavljenom B domenom | Liječenje hemofilije A |
| Czech | Adeno-asociovaný virový vektor sérotypu 8 obsahující funkční kopii kodonově optimalizované F8 cDNA kódující lidský koagulační faktor VIII s delecí B domény | Léčba hemofilie A |
| Danish | Adeno-associeret virus serotype 8-vektor, indeholdende en funktionel kopi af det kodon-optimerede F8 cDNA, der koder for B-domæne-slettet human koagulationsfaktor VIII | Behandling af hæmofili A |
| Dutch | Adeno-geassocieerd viraal vector serotype 8 dat een functionele kopie bevat van het codon-geoptimaliseerde F8 cDNA die codeert voor de humane stollingsfactor VIII met verwijderd B-domein | Behandeling van hemofilie A |
| Estonian | Inimese B-domeenita VIII hüübimisfaktori koodon-optimeeritud F8 cDNA funktsionaalset koopiat sisaldav adeno-assotsieerunud viirusvektori 8. serotüüp | Hemofiilia A ravi |
| Finnish | Adenoassosioitu serotyypin 8 virusvektori, joka sisältää funktionaalisen kopion kodonioptimoitua ihmisen hyytymistekijää VIII (F8 cDNA), josta on poistettu B-domeeni | Hemofilia A:n hoito |
| French | Vecteur viral adéno-associé de sérotype 8 contenant une copie fonctionnelle d'ADNc de F8 à codons optimisés codant pour le facteur VIII de coagulation humain dépourvu du domaine B | Traitement de l'hémophilie A |
| German | Adeno-assoziierter-Virus-Vektor Serotyp 8, der eine funktionelle Kopie der Codon-optimierten F8-cDNA enthält, die für den B-Domänen-deletierten humanen Gerinnungsfaktor VIII codiert | Behandlung der Hämophilie A |
| Greek | Αδενο-σχετιζόμενος ιικός φορέας οροτύπου 8 που περιέχει λειτουργικό αντίγραφο του F8 cDNA βελτιστοποιημένου κωδικονίου που κωδικοποιεί τον ανθρώπινο παράγοντα πήξης VIII διαγραμμένου τομέα B | Θεραπεία της αιμορροφιλίας A |
| Hungarian | Adeno-asszociált 8-as szerotípusú vírusvektor, amely a törölt B-doménű, VIII-as humán alvadási faktort kódoló kodon-optimalizált F8 cDNA funkcionális másolatát tartalmazza | A típusú hemofília kezelése |
| Italian | Vettore virale adeno-associato di sierotipo 8 contenente una copia funzionale del cDNA dell'F8 con ottimizzazione del codone codificante il fattore della coagulazione VIII umano con delezione del dominio B | Trattamento dell'emofilia A |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Latvian | Adeno-asociētā vīrusa vektora 8. stereotips, kas satur F8 cDNS funkcionālu kopiju ar optimizētu kodonu, kas kodē cilvēka VIII koagulācijas faktoru ar dzēstu B-domēnu | A tipa hemofilijas ārstēšana |
| Lithuanian | Adenoasocijuoto viruso vektoriaus serotipas 8, turintis funkcinę F8 cDNR optimizuoto kodono kopiją, koduojančią be B-domeno žmogaus VIII krešėjimo faktorių | Hemofilijos A gydymas |
| Maltese | Vettur ta' virus ta' serotip 8 assoċjat ma' adeno li fih kopja funzjonali tal-F8-cDNA ottimizzat minn kodon li jikkodifika l-fattur VIII tal-koagulazzjoni umana b'dominju B imħassar | Kura ta' l-emofilja A |
| Polish | Wektor wirusowy serotypu 8 związany z adenowirusami zawierający funkcjonalną kopię F8 cDNA ludzkiego czynnika krzepnięcia VIII po optymalizacji kodonu i pozbawionego domeny B | Leczenie hemofilii A |
| Portuguese | Vetor viral adeno-associado de serótipo 8 contendo uma cópia funcional do ADNc do F8 com codão otimizado que codifica o fator VIII da coagulação humana com domínio B truncado | Tratamento da hemofilia A |
| Romanian | Vector viral adeno-asociat de serotip 8 care conține o copie funcțională a F8 ADNc cu codon optimizat, care codifică factorul de coagulare uman VIII cu domeniul B eliminat | Tratamentul hemofiliei A |
| Slovak | Adeno-asociovaný vírusový vektor sérotypu 8 obsahujúci funkčnú kópiu faktora VIII komplementárnej DNA s optimalizovaným kodónom na kódovanie ľudského koagulačného faktora VIII bez B-domény | Liečba hemofílie A |
| Slovenian | Adenoasociacijski virusni vektor serotipa 8, ki vsebuje funkcionalno kopijo kodonsko optimizirane cDNA za F8, ki kodira humani koagulacijski faktor VIII z izbrisano domeno B | Zdravljenje hemofilije A |
| Spanish | Vector vírico adenoasociado de serotipo 8 que contiene una copia funcional del ADN circulante del F8 con codones optimizados que codifica el factor de coagulación VIII humano con el dominio B suprimido | Tratamiento de la hemofilia A |
| Swedish | Adenoassocierad viral vektor av serotyp 8 som innehåller en funktionell kopia av kodonoptimerat F8 cDNA som avkodar B-domändeleterad koagulationsfaktor VIII | Behandling av hemofili A |
| Norwegian | Adenoassosiert virusvektor serotype 8 som inneholder en funksjonell kopi av kodonoptimalisert F8 cDNA som koder for B-domene-slettet human koagulasjonsfaktor VIII | Behandling av hemofili A |
| Icelandic | Adenotengd veirugenaferja af sermisgerð 8 sem inniheldur virkt afrit af táknahámörkuðu F8 cDNA sem kóðar fyrir manna storkuþátt VIII með eyddu B-hneppi | Meðferð við dreyrasýki A |