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# Public summary of opinion on orphan designation

## Recombinant human coagulation factor VIII Fc – von Willebrand factor – XTEN fusion protein for the treatment of haemophilia A

On 28 June 2019, orphan designation EU/3/19/2176 was granted by the European Commission to Swedish Orphan Biovitrum AB (publ), Sweden, for recombinant human coagulation factor VIII Fc – von Willebrand factor – XTEN fusion protein (also known as BIVV001) for the treatment of haemophilia A.

### What is haemophilia A?

Haemophilia A is an inherited bleeding disorder caused by the lack of factor VIII, which is one of the proteins involved in blood coagulation (clotting). 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 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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) can produce 'inhibitors' (antibodies) against factor VIII which stop the factor VIII medicine from working. In these cases, different blood clotting factors or other treatments needed to be used, either alone or as part of a combination treatment.

*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 518,400,000 (Eurostat 2019).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with haemophilia A because preliminary results indicate that it can increase how long factor VIII remains in the blood. 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 A cannot make enough functioning factor VIII because the gene for producing the clotting factor is damaged.

This medicine is made up of a genetically engineered factor VIII protein attached to fragments from other proteins: von Willebrand factor and XTEN. When injected into the patient, it is expected that the proteins attached to factor VIII will make factor VIII remain longer in the bloodstream, thereby reducing the tendency for bleeding for a long time.

## 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 the treatment of haemophilia A. Orphan designation had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a Positive opinion on 23 May 2019, 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 | Recombinant human coagulation factor VIII Fc - von Willebrand factor - XTEN fusion protein | Treatment of haemophilia A |
| Bulgarian | Рекомбинантен човешки коагулационен фактор VIII Fc - фактор на von Willebrand - XTEN фузионен протеин | Лечение на хемофилия А |
| Croatian | Rekombinantni ljudski faktor koaglulacije VIII Fc - von Willebrandov faktor - XTEN fuzijski protein | Liječenje hemofilije A |
| Czech | Rekombinantní humánní koagulační faktor VIII Fc - von Willebrandův faktor - XTEN fuzní protein | Léčba hemofilie A |
| Danish | Rekombinant human koagulationsfaktor VIII Fc - von Willebrand-faktor - XTEN fusionsprotein | Behandling af hæmofili A |
| Dutch | Recombinant-humane-stollingsfactor VIII Fc - von willebrandfactor - XTEN fusie-eiwit | Behandeling van hemofilie A |
| Estonian | Rekombinantne inimese VIII hüübimisfaktor Fc - von Willebrandi faktor - XTEN liitvalk | Hemofiilia A ravi |
| Finnish | Rekombinantti hyytymistekijä VIII Fc - von Willebrandin-tekijä - XTEN fuusioproteiini | Hemofilia A:n hoito |
| French | Facteur VIII de coagulation humain recombinant fragment Fc - facteur von Willebrand - fusionné au fragment XTEN | Traitement de l'hémophilie A |
| German | Rekombinanter humaner Gerinnungsfaktor VIII Fc - von Willebrand Faktor - XTEN Fusionsprotein | Behandlung der Hämophilie A |
| Greek | Ανασυνδυασμένη πρωτεΐνη σύντηξης ανθρώπινου παράγοντα πήξης VIII Fc - παράγοντα von Willebrand - XTEN | Θεραπεία της αιμορροφιλίας Α |
| Hungarian | Rekombináns humán VIII as alvadási faktor Fc - von Willebrand-faktor - XTEN fúziós fehérje | A típusú hemofília kezelése |
| Italian | Fattore VIII della coagulazione umano ricombinante Fc - fattore di von Willebrand - proteina di fusione XTEN | Trattamento dell'emofilia A |
| Latvian | Rekombinanta cilvēka VIII koagulācijas faktora Fc - fon Villebranda faktora - XTEN fūzijas proteīns | A tipa hemofilijas ārstēšana |
| Lithuanian | Rekombinantinis žmogaus krešėjimo faktorius VIII, Fc - von Willebrand'o faktorius - XTEN suliejimo baltymas | Hemofilijos A gydymas |
| Maltese | Fattur VIII tal-koagulazzjoni umana rikombinanti Fc - l-fattur von Willebrand - proteina tal-fużjoni XTEN | Kura ta' l-emofilja A |
| Polish | Rekombinowany ludzki czynnik krzepnięcia VIII Fc - czynnika von Willebranda - białko fuzyjne XTEN | Leczenie hemofilii A |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Portuguese | Proteína de fusão composta pelo Fator VIII de coagulação humana recombinante Fc - fator de von Willebrand e polipeptido XTEN | Tratamento da hemofilia A |
| Romanian | Proteină de fuziune: factor VIII de coagulare uman recombinant Fc - factor von Willebrand – fragment XTEN | Tratamentul hemofiliei A |
| Slovak | Rekombinantný ľudský koagulačný faktor VIII Fc - von Willebrandov faktor - XTEN fúzny proteín | Liečba hemofílie A |
| Slovenian | Rekombinantni humani koagulacijski faktor VIII Fc - von Willebrandov faktor - fuzijska beljakovina XTEN | Zdravljenje hemofilije A |
| Spanish | Factor VIII de coagulación recombinante humano Fc - factor de von Willebrand - proteína de fusión XTEN | Tratamiento de la hemofilia A |
| Swedish | Rekombinant human koagulationsfaktor VIII Fc - von Willebrands faktor - XTEN fusionsprotein | Behandling av hemofili A |
| Norwegian | Rekombinant human koagulasjonsfaktor VIII Fc - von Willebrand faktor - XTEN fusjonsprotein | Behandling av hemofili A |
| Icelandic | Raðbrigða storkuþáttur manna VIII Fc - von Willebrand þáttur - XTEN samrunaprótein | Meðferð við dreyrasýki A |