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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin for the treatment of haemophilia B

On 22 August 2014, orphan designation (EU/3/14/1319) was granted by the European Commission to Richardson Associates Regulatory Affairs Ltd, United Kingdom, for recombinant factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin for the treatment of haemophilia B.

What is haemophilia B?

Haemophilia B is an inherited bleeding disorder that is caused by the lack of factor IX, which is one of the proteins 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. 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 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 0.2 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).

What treatments are available?

At the time of submission of the application for orphan drug designation, medicines containing factor IX were authorised in the EU for the treatment of haemophilia B, to replace the missing protein.

*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 511,100,000 (Eurostat 2014).

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However, not all patients with haemophilia B could benefit from these medicines because the immune system (the body's natural defences) can react against them by producing 'inhibitors' (antibodies) against factor IX. 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 B because it could be used in patients who have developed inhibitors against factor IX. The medicine is also expected to last longer inside the body and thus may be given less often than existing treatments. These assumptions 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 copy of human factor VIIa, to which a chain made of three copies of a fragment of the 'human chorionic gonadotropin' (hCG) hormone has been added. In the body, the medicine is expected to work in the same way as human factor VIIa. Factor VIIa is involved in blood clotting. It activates another factor called factor X, which starts the clotting process. By activating factor X, this medicine is expected to control the bleeding disorder in patients who have developed inhibitors to factor IX because it acts directly on factor X, independently of factor IX.

Attaching the hCG chain to factor VIIa is expected to decrease the rate at which the factor VIIa is cleared from the body, allowing injections to be given less frequently than medicines that contain only factor VII or VIIa.

The medicine is made by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce factor VIIa linked to a chain made of fragments of hCG.

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, no clinical trials with the medicine in patients with haemophilia B had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for haemophilia B. Orphan designation of the medicine had been granted in the United States for the treatment and prophylaxis of bleeding episodes in patients with haemophilia A or B with inhibitors.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 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:

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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 factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin	Treatment of haemophilia B
Bulgarian	Рекомбинантен фактор VIIa модифициран с три терминални повторения получени от β верига на човешки хорион гонадотропин	Лечение на хемофилия B
Croatian	Rekombinantni faktor VIIa modificiran s tri terminalna ponavljanja dobivena iz β-lanca ljudskog korionskog gonadotropina	Liječenje hemofilije B
Czech	Rekombinantní koagulačního faktoru VIIa upravené s třemi terminál opakuje z řetězce β lidský choriový gonadotropin	Léčba hemofilie B
Danish	Rekombinant koagulationsfaktor VIIa modificeret med tre terminale kopier stammende fra β-kæden af humant choriongonadotropin	Behandling af hæmofili B
Dutch	Recombinant stollingsfactor VIIa bewerkt met drie terminal herhalingen afgeleid van de β-keten van humaan choriongonadotrofine	Behandeling van hemofilie B
Estonian	Rekombinantne VIIa hüübimisfaktor, mida on modifitseeritud kolme terminaalkorduse osas saadud inimese kooriongonadotropiini β ahelast	Hemofiilia B ravi
Finnish	Rekombinantti hyytymistekijä VIIa, muunnettu kolmella ihmisperäisen koriongonadotropiinin β-ketjusta johdetun terminaalin toistolla	Hemofilia B:n hoito
French	Facteur VIIa recombinant modifié avec trois répétitions terminales dérivées de la chaîne β de la gonadotrophine chorionique humaine	Traitement de l'hémophilie B
German	Modifizierter rekombinanter Blutgerinnungsfaktor VIIa mit drei aus der β-Kette von humanem Choriongonadotropin abgeleiteten terminalen Repeats	Behandlung der Hämophilie B
Greek	Ανασυνδυασμένος παράγοντας VIIa τροποποιημένος με τρεις τερματικές επαναλήψεις που προέρχονται από τη β αλυσίδα της ανθρώπινης χοριακής γοναδοτροπίνης	Θεραπεία της αιμορροφιλίας B
Hungarian	Humán chorion gonadotropin β-láncából származó három terminális ismétlődéssel módosított rekombináns VIIa véralvadási faktor	B típusú hemofília kezelése
Italian	Fattore VIIa di coagulazione del sangue ricombinante modificato con tre ripetizioni terminali derivati dalla catena β della gonadotropina corionica umana	Trattamento dell'emofilia B
Latvian	Rekombinants VIIa asinsreces faktors, kas modificēts ar trim terminālie atkārtojumiem, kas iegūti no cilvēka horiongonadotropīna β ķēdes	B tipa hemofilijas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Rekombinantinis VIIa krešėjimo faktorius modifikuotas trimis terminaliniais pasikartojimais, išgautais iš žmogaus chorioninio gonadotropino β grandinės	Hemofilijos B gydymas
Maltese	Fattur VIIa rikombinanti modifikat bi tliet trufijiet ripetuti imnisslin mill-katina β tal-gonadotropina korjonika umana	Kura ta' l-emofilja B
Polish	Rekombinowany czynnik krzepnięcia VIIa zmodyfikowany trzema powtórzeniami terminalnymi otrzymanymi z łańcucha β ludzkiej gonadotropiny kosmówkowej	Leczenie hemofilii B
Portuguese	Fator VIIa da coagulação recombinante modificado com três repetições terminais derivadas da cadeia β da gonadotrofina coriónica humana	Tratamento da hemofilia B
Romanian	Factorul de coagulare VIIa recombinant modificat cu trei repetiţii terminale derivate din lanţul β al gonadotropinei corionice umane	Tratamentul hemofiliei B
Slovak	Rekombinantný koagulačný faktor VIIa upravený troma terminálnymi sekvenciami odvodenými z β reťazca ľudského chóriového gonadotropínu	Liečba hemofílie B
Slovenian	Rekombinantni koagulacijski faktor VIIa modificiran s tremi terminalnimi ponovitvami, ki izvirajo iz β verige humanega horionskega gonadotropina	Zdravljenje hemofilije B
Spanish	Factor VIIa de coagulacion recombinante modificada con tres repeticiones terminales derivadas de la cadena β de la gonadotropina coriónica humana	Tratamiento de la hemofilia B
Swedish	Rekombinant koagulationsfaktor VIIa modifierad med tre terminala upprepningar härledda från β-kedjan av humant koriongonadotropin	Behandling av hemofili B
Norwegian	Rekombinant koagulasjionsfaktor VIIa modifisert med tre terminale repeterende enheter avledet fra β-kjeden av humant koriongonadotropin	Behandling av hemofili B
Icelandic	Raðbrigða storkuþáttur VIIa breyttur með þremur endaendurtekningum dregnum af β keðju manna chóríónic gónadótrópíni	Meðferð við dreyrasýki B