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Public summary of opinion on orphan designation

Human monoclonal IgG2 antibody against tissue factor pathway inhibitor for the treatment of haemophilia A

On 22 February 2018, orphan designation (EU/3/18/1979) was granted by the European Commission to Bayer AG, Germany, for human monoclonal IgG2 antibody against tissue factor pathway inhibitor (also known as BAY 1093884) 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) 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

*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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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 early studies showed that the medicine works in patients who have developed inhibitors to authorised treatments. In addition, studies in experimental models suggest that the medicine may be safer than some authorised treatments, because it lowers the risk of clots in blood vessels.

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 a monoclonal antibody (a type of protein) that has been designed to recognise and attach to TFPI, a protein that blocks an alternative process for blood clotting which does not need factor VIII. By attaching to TFPI, the medicine is expected to prevent its activity and allow blood clotting by the alternative process in patients with haemophilia A. This is expected to reduce bleeding.

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 January 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	Human monoclonal IgG2 antibody against tissue factor pathway inhibitor	Treatment of haemophilia A
Bulgarian	Човешко моноклонално IgG2 антитяло срещу инхибитор на пътя на тъканния фактор	Лечение на хемофилия А
Croatian	Humano monoklonsko IgG2 protutijelo protiv inhibitora puta tkivnog faktora	Liječenje hemofilije A
Czech	Lidská monoklonální protilátka IgG2 proti inhibitoru dráhy tkáňového faktoru	Léčba hemofilie A
Danish	Humant monoklonalt IgG2-antistof mod Tissue Factor Pathway Inhibitor	Behandling af hæmofili A
Dutch	Humaan monoklonaal IgG2-antilichaam gericht tegen tissue factor pathway inhibitor (TFPI)	Behandeling van hemofilie A
Estonian	Koefaktori juhtetee inhibiitori vastane inimese monoklonaalne IgG2 antikeha	Hemofiilia A ravi
Finnish	Ihmisen monoklonaalinen IgG2-luokan vasta-aine kudostekijätien estäjää vastaan	Hemofilia A:n hoito
French	Anticorps monoclonal humain IgG2 dirigé contre l'inhibiteur de la voie du facteur tissulaire	Traitement de l'hémophilie A
German	Humaner monoklonaler IgG2 Antikörper gegen "Tissue Factor Pathway Inhibitor"	Behandlung der Hämophilie A
Greek	Ανθρώπινο μονοκλωνικό αντίσωμα IgG2 έναντι του αναστολέα της οδού του ιστικού παράγοντα	Θεραπεία της αιμορροφιλίας Α
Hungarian	Szöveti faktor útvonal inhibitor (TFPI) ellenes humán monoklonális IgG2 antitest	A típusú hemofília kezelése
Italian	Anticorpo umanizzato monoclonale IgG2 contro l'inibitore della via del fattore tissutale	Trattamento dell'emofilia A
Latvian	Cilvēka monoklonālā IgG2 antiviela, kas vērsta pret audu faktora signālceļu inhibitoru	A tipa hemofilijas ārstēšana
Lithuanian	Žmogaus monokloninis IgG2 antikūnas prieš audinių faktoriaus kelio inhibitorių	Hemofilijos A gydymas
Maltese	Antikorp monoklonali IgG2 uman kontra l-inibitur tar-rotta tal-fattur tat-tessut	Kura ta' l-emofilja A
Polish	Ludzkie przeciwciało monoklonalne IgG2 przeciwko inhibitorowi drogi krzepnięcia zależnej od czynnika tkankowego	Leczenie hemofilii A
Portuguese	Anticorpo monoclonal humano IgG2 contra o inibidor da via do fator tecidual (TFPI)	Tratamento da hemofilia A
Romanian	Anticorp monoclonal uman IgG2 împotriva inhibitorului căii factorului tisular	Tratamentul hemofiliei A
Slovak	Ľudská monoklonálna protilátka IgG2 proti inhibítoru dráhy tkanivového faktora	Liečba hemofílie A

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Humano monoklonsko protitelo IgG2 proti zaviralcu poti tkivnega faktorja	Zdravljenje hemofilije A
Spanish	Anticuerpo monoclonal humano IgG2 contra el inhibidor de la vía del factor tisular	Tratamiento de la hemofilia A
Swedish	Human monoklonal IgG2-antikropp mot Tissue Factor Pathway Inhibitor (TFPI)	Behandling av hemofili A
Norwegian	Humant monoklonalt IgG2-antistoff mot "tissue factor pathway inhibitor" (TFPI)	Behandling av hemofili A
Icelandic	Einstofna IgG2 mannamótefni gegn TFPI (tissue factor pathway inhibitor)	Meðferð við dreyrasýki A