8 March 2017
EMA/5825/2017
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous dendritic cells incubated ex vivo with zebularine and factor VIII for the treatment of haemophilia A

On 12 January 2017, orphan designation (EU/3/16/1813) was granted by the European Commission to Idogen AB, Sweden, for autologous dendritic cells incubated ex vivo with zebularine and factor VIII (also known as IN-3012) 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 the blood coagulation (clotting) process. Patients with haemophilia A are more prone to bleeding than normal and they bleed for a long time 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 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 haemophilia A benefitted from these medicines because the immune system (the body's natural defences) can regard the factor VIII medicines as 'foreign' and produce 'inhibitors' (antibodies) against factor VIII

[*]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).

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and thereby stop the 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 laboratory studies showed that it may improve 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?

The medicine is expected to work by preventing production of inhibitors against factor VIII, thereby improving the effectiveness of factor VIII medicines.

The medicine is prepared from the patient's own immune cells called dendritic cells. These cells are mixed in the laboratory with factor VIII and a substance known as zebularine. Fragments of factor VIII attach to the dendritic cell surfaces and zebularine activates proteins that stop the immune system from attacking 'foreign' substances. When these dendritic cells are injected back into the patient, it is expected that they will stop the patient's immune system from regarding factor VIII as 'foreign' and so prevent production of inhibitors against factor VIII.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with haemophilia A had been started.

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 8 December 2016 recommending the granting of this designation.

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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	Autologous dendritic cells incubated ex vivo with zebularine and factor VIII	Treatment of haemophilia A
Bulgarian	Автоложни дендритни клетки инкубирани ex vivo със зебуларин и фактор VIII	Лечение на хемофилия А
Croatian	Autologne dendritičke stanice inkubirane ex vivo zebularinom i faktorom VIII	Liječenje hemofilije A
Czech	Autologní dendritické buňky inkubované ex vivo se zebularinem a faktorem VIII	Léčba hemofilie A
Danish	Autologe dendritceller inkuberet *ex vivo* med zubularin og faktor VIII	Behandling af hæmofili A
Dutch	Autologe dendritische cellen geïncubeerd ex vivo met zebularine en factor VIII	Behandeling van hemofilie A
Estonian	Autoloogsed dendriidirakud, mida on inkubeeritud ex vivo koos zebulariini ja VIII hüübimisfaktoriga	Hemofiilia A ravi
Finnish	Autologiset dendriittisolut inkuboituina ex vivo yhdessä zebulariinin ja hyytymistekijä VIII:n kanssa	Hemofilia A:n hoito
French	Cellules dendritiques autologues incubées ex-vivo avec zébularine et facteur VIII	Traitement de l'hémophilie A
German	Autologe dendritische Zellen, ex vivo inkubiert mit Zebularin und Faktor III	Behandlung der Hämophilie A
Greek	Αυτόλογα δενδριτικά κύτταρα επωασμένα ex vivo με ζεμπουλαρίνη και παράγοντα VIII	Θεραπεία της αιμορροφιλίας Α
Hungarian	Zebularinnal és VIII-as faktorral ex vivo inkubált autológ dendritikus sejtek	A típusú hemofília kezelése
Italian	Cellule dendritiche autologohe incubate ex vivo con zebularina e fattore VIII	Trattamento dell'emofilia A
Latvian	Autologas dendrītiskās šūnas, kas inkubētas *ex vivo* ar zebularīnu un VIII faktoru	A tipa hemofilijas ārstēšana
Lithuanian	Autologinės dendritinės ląstelės inkubuotos *ex vivo* su zebularinu ir VIII faktoriumi	Hemofilijos A gydymas
Maltese	Ċelloli dendritiċi awtologi inkubati ex vivo biż-żebularina u l-fattur VIII	Kura ta' l-emofilja A
Polish	Autologiczne komórki dendrytyczne inkubowane ex vivo z zebularyną oraz czynnikiem VIII	Leczenie hemofilii A
Portuguese	Células dendríticas autólogas incubadas ex vivo com zebularina e fator VIII	Tratamento da hemofilia A
Romanian	Celule dendritice autologe incubate ex vivo cu zebularină şi factor VIII	Tratamentul hemofiliei A
Slovak	Autológne dendritické bunky inkubované ex vivo so zebularínom a faktorom VIII	Liečba hemofílie A

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Avtologne dendritične celice, inkubirane ex vivo z zebularinom in faktorjem VIII	Zdravljenje hemofilije A
Spanish	Celulas dendriticas autologas incubadas ex vivo en zebularina y Factor VIII.	Tratamiento de la hemofilia A
Swedish	Autologa dendritiska celler ex vivo inkuberade med zebularin och faktor VIII	Behandling av hemofili A
Norwegian	Autologe dendrittiske celler inkubert ex vivo med zebularin og faktor VIII	Behandling av hemofili A
Icelandic	Samgena griplu frumur inkúberaðar ex vivo með zebúlaríni og storkuþætti VIII	Meðferð við dreyrasýki A