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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Human plasma-derived alpha-1 proteinase inhibitor for the treatment of graft-versus-host disease

On 19 March 2015, orphan designation (EU/3/15/1455) was granted by the European Commission to Richardson Associates Regulatory Affairs Ltd, United Kingdom, for human plasma-derived alpha-1 proteinase inhibitor for the treatment of graft-versus-host disease.

What is graft-versus-host disease?

Graft-versus-host disease (GvHD) is a complication that can affect patients who have received allogeneic haematopoietic (blood) stem-cell transplantation. This is a complex procedure used to treat diseases such as leukaemia (a cancer of the white blood cells), whereby a patient receives stem cells from a matched donor to help restore the bone marrow, which produces new blood cells.

In GvHD, the transplanted cells recognise the patient as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. GvHD may happen shortly after transplantation or later on, in which case a wider range of organs can be involved. GvHD is a serious and life-threatening disease with a high mortality rate.

What is the estimated number of patients affected by the condition?

At the time of designation, GvHD affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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, several medicines were authorised in the European Union (EU) for the prevention of GvHD and ciclosporin and corticosteroids were used to treat patients who developed the

*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 512,900,000 (Eurostat 2015).

condition. Treatment aimed at reducing the activity of immune cells involved in GvHD, thereby reducing their ability to attack the patient's organs.

The sponsor has provided sufficient information to show that human plasma-derived alpha-1 proteinase inhibitor might be of significant benefit for patients with GvHD because early results suggest that it can improve symptoms in patients who develop GvHD and who do not respond to treatment with corticosteroids and prevention with cyclosporin. 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?

Human plasma-derived alpha-1 proteinase inhibitor is a natural protein derived from human blood that blocks the action of a group of enzymes called serine proteases. These enzymes, which include neutrophil elastase, trypsin and proteinase-3, help to break up proteins in the body and have an important role in the processes of inflammation and cell death that are triggered in GvHD. By blocking their action, the medicine is expected to improve the symptoms of the condition and reduce organ damage.

What is the stage of development of this medicine?

The effects of human plasma-derived alpha-1 proteinase inhibitor 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 GvHD were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for GvHD or designated as an orphan medicinal product elsewhere for this condition. The medicine was available in the United States for the treatment of emphysema due to congenital deficiency of alpha-1 proteinase inhibitor (a lung disease caused by an inherited lack of the active substance in this medicine).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 February 2015 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Human plasma-derived alpha-1 proteinase inhibitor	Treatment of graft-versus-host disease
Bulgarian	Алфа-1 протеиназен инхибитор получен от човешка плазма	Лечение на болестта на присадката срещу приемателя
Croatian	Inhibitor alfa-1 proteinaze dobiven iz ljudske plazme	Liječenje reakcije presatka protiv primatelja
Czech	Alfa-1 proteinázy inhibitor pocházející z lidské plazmy	Léčba reakce štěpu proti hostiteli
Danish	Humant plasma-afledt alfa-1-proteinasehæmmer	Behandling af graft versus host reaktion
Dutch	Humaan plasma afgeleide alfa-1 proteïnase remmer	Behandeling van graft versus host ziekte
Estonian	Inimese plasmast saadud alfa-1 proteinaasi inhibiitor	Graft versus host haiguse ravi
Finnish	Ihmisplasmasta peräisin oleva alfa-1 proteinaasinestäjä	Käänteishyljintäreaktion hoito
French	Inhibiteur de la protéinase alpha-1 dérivée du plasma humain	Traitement de la réaction du greffon contre l'hôte
German	Alpha-1-Proteinase-Inhibitor aus humanem Plasma	Behandlung der Graft-versus-Host-Reaktion
Greek	Αναστολέας άλφα-1 πρωτεϊνάσης προερχόμενος από ανθρώπινο πλάσμα	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	Az emberi vérplazmából származó alfa-1 proteináz inhibitor	Graft-versus-host betegség kezelése
Italian	Inibitore della proteasi alfa-1 derivato dal plasma umano	Trattamento della reazione del trapianto contro l'ospite
Latvian	No cilvēka plazmas iegūts alfa-1 proteināzes inhibitors	Saimnieka-transplantāta slimības ārstēšana
Lithuanian	Alfa-1 proteinazės inhibitorius, išskirtas iš žmogaus plazmos	Transplantato atmetimo ligos gydymas
Maltese	Inibitur tal-alfa-1 proteinase imnissel mill-plażma umana	Kura tal-marda tat-tessut għat-trapjant kontra dak li jircievih
Polish	Inhibitor alfa-1-proteinazy otrzymany z ludzkiego osocza	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Inibidor da alfa-1 proteinase derivada do plasma humano	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Inhibitor al proteinazei alfa-1 derivat din plasmă umană	Tratamentul reacției grefei contra gazdei
Slovak	Alfa-1 proteinázový inhibítor pochádzajúci z ľudskej plazmy	Liečba reakcie štepú proti hostiteľovi

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Inhibitor proteinaze alfa-1, pridobljen iz človeške plazme	Zdravljenje bolezni presadka proti gostitelju
Spanish	Inhibidor de la alfa-1 proteinasa derivada de plasma humano	Tratamiento de la enfermedad de injerto contra huésped
Swedish	Alfa-1-proteinashämmare från human plasma	Behandling av graft-värd host reaktion
Norwegian	Human plasmaderivert alfa-1-proteinasehemmer	Behandling av graft-versus-host - reaksjon
Icelandic	Manna plasma-afleiddur alfa-1 próteinasahemill	Til meðferðar á hýsilssótt