



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human type I pancreatic elastase for the prevention of arteriovenous access dysfunction in haemodialysis patients

On 16 January 2014, orphan designation (EU/3/13/1218) was granted by the European Commission to Proteon Therapeutics Limited, United Kingdom, for recombinant human type I pancreatic elastase for the prevention of arteriovenous access dysfunction in haemodialysis patients.

What is arteriovenous access dysfunction?

Arteriovenous access dysfunction occurs when blood vessels that are used for haemodialysis become blocked. Haemodialysis is a technique used to clear waste products (such as urea) from the blood of patients whose kidneys are not working properly, since their kidneys are not able to perform this function.

Patients undergoing haemodialysis usually have two needles inserted into a blood vessel in the arm: one to draw the blood out, and one to return the purified blood back to the patient. This blood vessel is surgically prepared beforehand to provide a good blood flow. However, following the surgery a narrowing can develop which can block the access to the blood vessels. If the narrowing becomes severe, the access closes and haemodialysis can no longer be carried out effectively.

Arteriovenous access dysfunction is a long-term debilitating and potentially life-threatening condition because it makes the dialysis less effective and can lead to further damage to the kidneys.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients undergoing haemodialysis at risk of arteriovenous access dysfunction was estimated to be approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 102,000 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).

*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 512,200,000 (Eurostat 2013).



What treatments are available?

At the time of designation, there were no satisfactory methods authorised in the EU for the prevention of arteriovenous access dysfunction in haemodialysis patients. Some patients with arteriovenous access dysfunction were treated with angioplasty (a procedure to unblock blood vessels) to improve access or surgery to create a new access.

How is this medicine expected to work?

The medicine consists of a copy of the enzyme type I pancreatic elastase. This enzyme breaks down the elastin fibres in the blood vessel wall, which may inhibit the process of thickening of cell walls that causes blockage of the blood vessels.

The medicine is to be dripped onto the blood vessels by the surgeon immediately after access has been created for haemodialysis. As the medicine breaks down the elastin before it can encourage the thickening of blood vessel walls, it is expected to be able to help reduce the risk of the blood vessels becoming blocked, thereby preventing access dysfunction in patients undergoing haemodialysis.

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, clinical trials with the medicine in patients undergoing haemodialysis were completed and additional studies were planned.

At the time of submission, the medicine was not authorised anywhere in the EU for preventing arteriovenous access failure in haemodialysis patients. Orphan designation of the medicine has been granted in the United States for the 'prevention of arteriovenous fistula and arteriovenous graft failure in patients with chronic kidney disease who are receiving hemodialysis or preparing for hemodialysis'.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 November 2013 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	Recombinant human type I pancreatic elastase	Prevention of arteriovenous access dysfunction in haemodialysis patients
Bulgarian	Рекомбинантна човешка панкреасна еластаза от тип I	Превенция на артериовенозен достъп дисфункция при пациенти на хемодиализа
Czech	Rekombinantní lidská pankreatická elastáza typu I	Prevence dysfunkce arteriovenózního přístupu u dialyzovaných nemocných
Croatian	Rekombinantna ljudska pankreatična elastaza tipa I	Prevenција disfunkcije arteriovenskog pristupa u bolesnika na hemodijalizi
Danish	Rekombinant human type I pankreas-elastase	Forebyggelse af dysfunktion af den arteriovenøse adgang hos hæmodialyse patienter
Dutch	Recombinant humaan type 1 pancreas-elastase	Preventie van arterioveneuze toegangsdysfunctie in hemodialysepatiënten
Estonian	Rekombinantne inimese kõhunäärme 1. tüüpi elastaas	Arteriovenoosse ligipääsu düsfunktsiooni ennetamine hemodialüüsi patsientidel
Finnish	Ihmisen tyypin I rekombinanttinen haiman elastaasi	Hemodialyysipotilaan valtimo-laskimofistelin tukkeutumisen ehkäisy
French	Élastase pancréatique humaine recombinante de type I	Prévention du dysfonctionnement de l'accès artérioveineux chez des patients hémodialisés
German	Rekombinante humane Pankreas-Elastase Typ I	Prävention der Fehlfunktion eines arteriovenösen Zugangs bei Hämodialyse-Patienten
Greek	Ανασυνδυασμένη ανθρώπινη παγκρεατική ελαστάση Τύπου I	Πρόληψη δυσλειτουργίας της αρτηριοφλεβικής πρόσβασης σε ασθενείς αιμοδιάλυσης
Hungarian	Rekombináns humán 1-es típusú pankreász elasztáz	Arteriovenozus fisztula dysfunkciójának megelőzése haemodializisre szoruló betegeknél
Italian	Elastasi pancreatica umana ricombinante di tipo I	Prevenzione della disfunzione di accesso artero-venoso nei pazienti in emodialisi
Latvian	Rekombinanta cilvēka I tipa pankreātiskā elastāze	Arteriovenozās piekļuves traucējumu profilakse hemodialīzes pacientiem
Lithuanian	Rekombinantinė žmogaus I tipo pankreatinė elastazė	Arterioveninio priepuolio disfunkcijos prevencija hemodializuojamiems pacientams
Maltese	Elastasi tal-frixa tat-tip I uman rikombinanti	Prevenzjoni ta' taħsir ta' funzjoni tal-aċċess arterjovenuż f'pazjenti fl-emodijalisi

¹ At the time of designation

Language	Active ingredient	Indication
Polish	Rekombinowana ludzka elastaza trzustkowa typu I	Zapobieganie dysfunkcji dostępu naczyniowego u pacjentów dializowanych
Portuguese	Elastase pancreática humana recombinante de tipo I	Prevenção da disfunção do acesso arteriovenoso em doentes a fazer hemodiálise
Romanian	Elastază pancreatică umană recombinantă de tip I	Prevenirea disfuncției căii de acces arterio-venoase la pacienții supuși hemodializei
Slovak	Rekombinantná ľudská pankreatická elastáza typu I	Prevencia dysfunkcie artériovenózneho prístupu u hemodialyzovaných pacientov
Slovenian	Rekombinantna humana pankreatična elastaza tipa I	Preprečevanje disfunkcije arteriovenskega pristopa pri bolnikih na hemodializi
Spanish	Elastasa pancreática humana recombinante de tipo I	Prevención del fallo del acceso arteriovenoso en los pacientes en hemodiálisis
Swedish	Rekombinant humant pankreaselastas typ 1	Förebyggande av arteriovenös tillgångsdysfunktion hos dialyspatienter
Norwegian	Rekombinant human pankreaselastase av type I	Forebygging av arteriovenøs tilgangsdysfunksjon hos hemodialyse-trengende pasienter
Icelandic	Raðbrigða manna briselastasi af gerð I	Til varnar vanvirkni á slagæða-bláæðatengingu hjá sjúklingum í blóðskilun