European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF pancreatic enzymes (cross linked enzyme crystal lipase, protease, amylase) for the treatment of malabsorption due to exocrine pancreatic enzyme insufficiency

On 2 September 2004, orphan designation (EU/3/04/222) was granted by the European Commission to Dr Falk Pharma GmbH, Germany, for pancreatic enzymes (cross linked enzyme crystal lipse, protease, amylase) for the treatment of malabsorption due to exocrine pancreatic enzyme insufficiency.
The sponsorship was transferred to Gregory Fryer Associates Ltd, United Kingdom, in June 2008.

What is malabsorption due to exocrine pancreatic enzyme insufficiency?

The pancreas is a small organ that lies behind the stomach and in front of the spine. The pancreas has two main functions in the body. It makes hormones, such as insulin, that help to control blood sugar levels (this is called endocrine activity). It also makes a juice that helps to digest (break down) food (this is called exocrine activity). The juice contains enzymes, which are proteins that speed up the transformation of certain substances (such as particles of food) into other substances.
Certain conditions affecting the pancreas, including cystic fibrosis, inflammation of the pancreas (pancreatitis), cancer of the pancreas and an inherited disease called Shwachman-Diamond syndrome, may interfere with its exocrine activity by reducing the synthesis and the release of pancreatic enzymes. This may result in a defective absorption (malabsorption) of food nutrients. Typically, the patient experiences bloating and pain in the abdominal area and loose, frequent stools. Malabsorption due to exocrine pancreatic enzyme insufficiency is a severe chronically debilitating condition.

What are the methods of treatment available?

Several pancreatic enzyme extracts were authorised for treatment of the condition at the time of application. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that the medicinal product might be of potential significant benefit for the treatment of malabsorption due to exocrine pancreatic insufficiency because it may have better efficacy than other available enzymes. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, malabsorption due to exocrine pancreatic enzyme insufficiency was considered to affect approximately 3.6 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 166,000 persons.
According to the information provided by the sponsor, malabsorption due to exocrine pancreatic enzyme insufficiency was considered to affect about 166,000 persons in the European Union.

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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How is this medicinal product expected to act?
The proposed medicinal product contains the following 3 enzymes: crystal lipase, protease and amylase. By administration of this product it is expected that it will substitute the lacking pancreatic enzymes and ultimately restore normal digestion.

What is the stage of development of this medicinal product?
The effects of pancreatic enzymes (cross linked enzyme crystal lipase, protease, amylase) were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with malabsorption due to exocrine pancreatic insufficiency were ongoing.

Pancreatic enzymes (cross linked enzyme crystal lipase, protease, amylase) were not marketed anywhere worldwide for malabsorption due to exocrine pancreatic insufficiency, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 22 July 2004 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pancreatic enzymes (cross linked enzyme crystal lipase, protease, amylase)	Treatment of malabsorption due to exocrine pancreatic enzyme insufficiency
Czech	Pankreatické enzymy (směs síťované krystalické lipázy, proteázy a amylázy)	Léčba malabsorpce při exokrinní insuficienci pankreatu
Danish	Pankreasenzymer (krydsbundet enzym krystal lipase, protease, amylase)	Behandling af malabsorption på grund af eksokrin pankreasenzyminsufficiens
Dutch	Pancreasenzymen ("cross-linked" lipase enzymkristal, protease, amylase)	Behandeling van malabsorptie ten gevolge van exocriene pancreasenzyminsufficiëntie
Estonian	Pankrease ensüümid (siduv ensüüm-kristall lipaas, proteaas, amülaas)	Pankrease eksokriinsete ensüümide puudulikkusest tingitud malabsorptsiooni ravi
Finnish	Haimaentsyymejä (silloitettu entsyymi kristalli lipaasi, proteaasi, amylaasi)	Imeytymishäiriön hoito, kun aiheuttajana on eksokriinisten haimaentsyymien vajaatoiminta
French	Enzymes pancréatiques (lipase sous forme cristalline, protéase, amylase)	Traitement des malabsorptions dues à une insuffisance pancréatique exocrine
German	Pankreasenzyme (gekoppeltes Lipasekristall, Protease, Amylase)	Behandlung der durch eine exokrin-pankreatische Enzyminsuffizienz verursachten Malabsorption
Greek	Παγκρεατικά ένζυμα (διασυνδεδεμένη ενζυμική κρυσταλλική λιπάση, πρωτεάση, αμυλάση)	Θεραπεία της δυσαπορρόφησης λόγω εξωκρινούς παγκρεατικής ενζυμικής ανεπάρκειας
Hungarian	Hasnyálmirigy enzimek (keresztkötésben lévő lipáz, proteáz, amiláz kristály)	Hasnyálmirigy exocrin enzimhiány okozta felszívódási zavar kezelése
Italian	Enzimi pancreatici (lipasi sotto forma di enzima cristallizzato con legami crociati, proteasi, amilasi)	Trattamento del malassorbimento dovuto a carenza degli enzimi pancreatici esocrini
Latvian	Aizkuņģa dziedzera enzīmi (šķērssūtā enzīma kristāla lipāze, proteāze, amilāze)	Ierobežotas absorbcijas ārstēšanai sakarā ar eksokrīnā aizkuņģa dziedzera enzīmu nepietiekamību
Lithuanian	Kasos fermentai (fermento kristalinės lipazės, proteazės, amilazės mišinys)	Malabsorbcijos dėl egzokrininės kasos funkcijos nepakankamumo gydymas
Maltese	Pancreatic enzymes (cross linked enzyme crystal lipase, protease, amylase)	Treatment of malabsorption due to exocrine pancreatic enzyme insufficiency
Polish	Enzymy trzustkowe (lipaza krystaliczna poprzecznie sieciowana, proteaza, amylaza)	Leczenie zaburzeń wchłaniania-powodowanych zewnątrzwydzielniczą niewydolnością trzustki
Portuguese	Enzimas pancreáticas (lipase cristalina de ligação cruzadas, protease, amilase)	Tratamento da mal-absorção devido a insuficiência enzimática pancreática exócrina
Slovak	Pankreatické enzýmy (vzájomne prepojený enzýmový kryštál lipázy, proteázy, amylázy)	Liečba porúch vstrebávania pre exokrinnú pankreatickú insuficienciu
Slovenian	Pankreasni encimi (prečno povezan	Zdravljenje malabsorpcije zaradi pomanjkanja

	encimski kristal lipaze, proteaze, amilaze)	eksokrinih pankreasnih encimov
Spanish	Enzimas pancreáticas (lipasa cristalina con puentes de unión, proteasa, amilasa)	Tratamiento de la malabsorción debida a insuficiencia enzimática pancreática exocrina.
Swedish	Pankreasenzymer (korsbundna enzym kristall lipas, proteas, amylas)	Behandling av malabsorption beroende på bristande funktion av enzymer från exokrina pankreas
Norwegian	Pankreasenzymer (kryssbundet krystallinsk lipase, protease, amylase)	Behandling av malabsorpsjon pga eksokrin sekretorisk pankreasinsuffisiens
Icelandic	Ensím briskirtils (lípasi, próteasi, amýlasi)	Til meðhöndlunar á vanupptöku vegna skorts á útkirtilsensímum brisins