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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 recombinant human CXCL8 mutant for the prevention of delayed graft function after solid organ transplantation

On 22 September 2008, orphan designation (EU/3/08/570) was granted by the European Commission to ProtAffin Biotechnologie AG, Austria, for recombinant human CXCL8 mutant for the prevention of delayed graft function after solid organ transplantation.

What is delayed graft function after solid organ transplantation?
Delayed graft function (DGF) is a complication that occurs in the first few days after the transplant of a solid organ, such as a kidney, when the transplanted organ does not start to work properly. DGF may be caused by events occurring after the restoration of blood flow to the transplanted organ. The damage to the organ caused by the interruption and restoration of blood flow is called ischaemia/reperfusion injury and is associated with an inflammatory reaction, characterised by the invasion of neutrophils (a type of white blood cell) into the transplanted organ. DFG is a life-threatening condition because of the risk of losing the transplanted organ.

What is the estimated number of patients at risk of developing the condition?
At the time of designation the population at risk of developing delayed graft function after solid organ transplantation was approximately 0.55 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 28,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of prevention are available?
At the time of submission of the application for orphan drug designation, there were no medicinal products in the Community for the prevention of DGF after solid organ transplantation. Several preventative measures were commonly used to reduce the risk of DGF, including careful selection of the organ donor and preservation of the organ during transport.
The sponsor has provided satisfactory argumentation to justify the assumption that recombinant human CXCL8 mutant might be of potential significant benefit for the prevention of DGF after solid organ transplantation, mainly because it has a novel mechanism of action that is expected to result in better efficacy. This assumption will need to be confirmed at the time of marketing authorisation, to maintain the orphan status.

How is this medicine expected to work?
Recombinant human CXCL8 mutant is similar to the human protein CXCL8 (previously called interleukin 8). In the body, CXCL8 goes to the sites of inflammation, such as newly transplanted

[*]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 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

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organs affected by ischaemia/reperfusion injury, where it attracts neutrophils. Recombinant human CXCL8 mutant replaces natural CXCL8 at the site of inflammation, but it is not able to attract neutrophils. By replacing CXCL8 at the site of the transplanted organ, recombinant human CXCL8 mutant is expected to prevent the infiltration of neutrophils into the organ, lowering the risk of DGF.

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 recombinant human CXCL8 mutant in experimental models was ongoing. No clinical trials in patients with solid organ transplantation had been started.

At the time of submission, recombinant human CXCL8 mutant was not authorised anywhere in the world for the prevention of DGF after solid organ transplantation, or designated as orphan medicinal product elsewhere for this condition.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted a positive opinion on 9 July 2008 recommending the granting of the above-mentioned 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 Community) 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.

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Patients' association contact point: Not available

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

Language	Active Ingredient	Indication
English	Recombinant human CXCL8 mutant	Prevention of delayed graft function after solid organ transplantation
Bulgarian	Рекомбинантен човешки CXCL8 мутант	Предотвратяване на забавено функциониране на присадката при органна трансплантация
Czech	Rekombinantní lidský CXCL8 mutatovaný	prevence opožděné funkce štěpu po transplantaci orgánu
Danish	Rekombinant human CXCL8 mutant	Forebyggelse af forsinket transplanteringsfunktion i forbindelse med organtransplantation
Dutch	Recombinante humane CXCL8-mutant	Preventie van vertraagde orgaan transplantaatfunctie
Estonian	Rekombinantne inimese CXCL8 mutant	Transplantaadi funktsiooni hilinemise tõkestamine pärast elundisiirdamist
Finnish	Yhdistelmä-DNA-tekniikalla valmistettu ihmisen CXCL8-mutantti	Siirrännäisen toimintaviiveen ehkäisy elinsiirrossa
French	CXCL8 humaine recombinante mutée	Prévention des retards fonctionnels du greffon dans la greffe d'organe.
German	Rekombinante humane CXCL8 Mutante	Vorbeugung der verzögerten Transplantatfunktion nach Organtransplantation
Greek	Ανασυνδυασμένος ανθρώπινος μεταλλάκτης CXCL8	Πρόληψη της αργοπορημένης λειτουργίας του μοσχεύματος κατά τη μεταμόσχευση οργάνων
Hungarian	Rekombináns humán CXCL8 mutáns	Szervtranszplantációt követő késői graftfunkció megelõzése
Italian	CXCL8 mutante ricombinante umano	Prevenzione del ritardo nella funzionalita' nell'organo trapiantato
Latvian	Cilvēka rekombinants CXCL8 mutants	Aizkavētas transplantāta funkcijas profilaksei pēc parenhimatozo orgānu transplantācijas
Lithuanian	Žmogaus rekombinantinis CXCL8 mutantas	Vėlyvos transplantato atmetimo reakcijos prevencija po organo transplantavimo
Maltese	Mutant taċ-CXCL8 rikombinanti uman	Prevenzjoni ta' ttardjar fil-funzjonalità ta' trapjant wara trapjant ta' organu
Polish	Rekombinowany ludzki CXCL8 mutant	Zapobieganie opóźnieniu podjęcia czynności przez przeszczepiony narząd
Portuguese	Mutante de CXCL8 humano recombinante	Prevenção do atraso funcional do órgão transplantado
Romanian	CXCL8 uman recombinant mutant	Prevenirea întârzierii funcționării grefei de organ transplantat
Slovak	Rekombinantný ľudský CXCL8-mutant	Prevencia oneskorenej funkcie štepu po transplantácii orgánu
Slovenian	Rekombinantni humani mutant CXCL8	Preprečevanje zapoznelega začetka delovanja presadka po presaditvi organa
Spanish	Mutante CXCL8 humano recombinante	Prevención del retraso de la función del órgano transplantado
Swedish	Rekombinant human CXCL8-mutant	Förebyggande av fördröjd transplantatfunktion i samband med organtransplantation

Norwegian	Rekombinant human CXCL8 mutant	Forebyggelse av forsinket transplantatfunksjon i forbindelse med organtransplantasjon
Icelandic	Raðbrigða manna CXCL8 stökkbrigði	Til að koma í veg fyrir síðkomna starfsbilun eftir líffæraígræðslu