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 recombinant human monoclonal antibody against transforming growth factor beta-1, 2 and 3 for the treatment of idiopathic pulmonary fibrosis

On 1 April 2008, orphan designation (EU/3/08/533) was granted by the European Commission to Genzyme BV, The Netherlands, for recombinant human monoclonal antibody against transforming growth factor beta-1, 2 and 3 for the treatment of idiopathic pulmonary fibrosis.

What is idiopathic pulmonary fibrosis?
Fibrosis is the formation of scar tissue as part of the natural repair process of the body following tissue damage. Idiopathic pulmonary fibrosis is thought to consist of a chronic inflammation (a response of the body to the injury caused to the tissue) and progressive formation of fibrous tissue in the walls of the small chambers containing air in the lungs. Since the injury causing these changes is unknown, it is called idiopathic. The progressive formation of scars impairs the normal functions of lung tissue, which are to enable exchange of oxygen and carbon dioxide between air and blood. The symptoms developed are persistent cough, progressive severe shortness of breath and recurrent lung infections.
Idiopathic pulmonary fibrosis is a chronically debilitating and life threatening disease due to the progression of respiratory symptom and complications, and short life expectancy.

What are the methods of treatment available?
No satisfactory methods exist that were authorised at the time of application. Only symptomatic treatments were used (such as corticosteroids and medicinal products that suppress the immune system) at the time of the submission of the application. In some patients, lung transplantation was performed.

What is the estimated number of patients affected by idiopathic lung fibrosis[*]?
Based on the information provided by the sponsor and previous knowledge of the Committee, idiopathic lung fibrosis was considered to affect approximately 2.7 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 134,000 persons.

How is this medicinal product expected to act?
Transforming growth factor beta (TGF beta) is a protein that can develop multiple functions. This protein comes in three forms (TGF beta-1, 2 and 3). TGF beta plays a specific role in accumulation of connective tissue that is important for scarring and wound healing. In idiopathic pulmonary fibrosis, these processes are abnormally high and lead to increased fibrosis. Therefore, it is thought that the excess fibrosis can be modified by blocking TGF beta.

[*] 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 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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Antibodies are proteins in the body that can identify and neutralize specific targets, and they are normally used by the immune system. Recombinant human monoclonal antibody against transforming growth factor beta-1, 2 and 3 is an antibody artificially produced that is able to recognise and block all three forms of TGFβ.

What is the stage of development of this medicinal product?
The effects of recombinant human monoclonal antibody against transforming growth factor beta-1, 2 and 3 were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with idiopathic lung fibrosis were ongoing.

Human monoclonal antibody against transforming growth factor beta-1, 2 and 3 was not authorised anywhere worldwide for idiopathic pulmonary fibrosis, at the time of submission.

Orphan designation of human monoclonal antibody against transforming growth factor beta-1, 2 and 3 was granted in the United States for idiopathic pulmonary fibrosis.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 6 February 2008 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	Recombinant human monoclonal antibody against transforming growth factor beta-1, 2 and 3	Treatment of idiopathic pulmonary fibrosis
Bulgarian	Рекомбинантно човешко моноклонално антитяло срещу трансформиращ растежен фактор бета 1, 2 и 3	Лечение на идиопатична белодробна фиброза
Czech	Rekombinantní humánní monoklonální protilátka proti transformujícímu růstovému faktoru (TGF) ß1,2 a 3	Léčba idiopatické plicní fibrózy
Danish	Rekombinant humant monoklonalt antistof mod Transforming Growth Factor beta 1, 2 og 3	Behandling af idiopatisk lungefibrose
Dutch	Recombinant humaan monoklonaal antilichaam gericht tegen transformerende groeifactor beta 1, 2 en 3	Behandeling van idiopathische longfibrose
Estonian	Rekombinantne inimese monoklonaalne antikeha transformeeriva kasvufaktori β-1, -2 ja -3 vastu	Idiopaatilise kopsufibroosi ravi
Finnish	Rekombinantti ihmisen monoklonaalinen vasta-aine transformoivaa kasvutekijä ß1,2 ja 3:a vastaan	Idiopaattisen keuhkofibroosin hoito
French	Anticorps monoclonal humain recombinant dirigé contre le Transforming Growth Factor ß 1, 2 et 3	Traitement de la fibrose pulmonaire idiopathique
German	Rekombinanter humaner monoklonaler Antikörper gegen Transformierenden Wachstumsfaktor beta1, 2 und 3	Behandlung von Idiopathischer Pulmonaler Fibrose
Greek	Ανθρώπινο ανασυνδυασμένο μονοκλωνικό αντίσωμα εναντίον του Μετατροπέα Αυξητικού Παράγοντα β 1,2 και 3	Θεραπεία της ιδιοπαθούς πνευμονικής ίνωσης
Hungarian	Rekombináns humán monoklonális antitest a β1, 2 és 3 transzformáló növekedési faktor (TGF) ellen	Idiopathiás tüdőfibrózis kezelése
Italian	Anticorpo monoclonale umano ricombinante anti-TGF ß1, 2 e 3	Trattamento della fibrosi polmonare idiopatica
Latvian	Cilvēka rekombinantā monoklonālā antiviela pret transformējošo augšanas faktoru β-1, β-2 un β-3	Idiopātiskās plaušu fibrozes ārstēšana
Lithuanian	Rekombinantinis žmogaus monokloninis antikūnas prieš transformuotą augimo faktorių β-1, 2 ir 3	Idiopatinės plaučių fibrozės gydymas
Maltese	Anti-korp uman monoklonali rikombinanti kontra l-fattur li jbiddel l-iżvilupp tat-tip beta 1, 2 u 3	Kura tal-fibrożi pulmonari idjopatika

Polish	Rekombinowane ludzkie przeciwciało monoklonalne przeciwko przekształconemu czynnikowi wzrostowemu ß1, 2 i 3	Leczenie idiopatycznego zwłóknienia płuc
Portuguese	Anticorpo monoclonal humano recombinante específico para TGF ß (factor beta de transformação do crescimento) 1, 2 e 3	Tratamento da fibrose pulmonar idiopática
Romanian	Anticorp monoclonal uman recombinant anti factor transformator de creştere beta 1, 2 şi 3	Tratamentul fibrozei pulmonare idiopatice
Slovak	Rekombinantná humánna monoklonálna protilátka proti transformujúcemu rastovému faktoru (TGF) ß 1, 2 a 3	Liečba idiopatickej pľúcnej fibrózy
Slovenian	Rekombinantno humano monoklonsko protitelo proti TGF ß1, 2 in 3	Zdravljenje idiopatske pljučne fibroze
Spanish	Anticuerpo monoclonal humano recombinante contra el factor transformador del crecimiento (TGF) ß1, 2 y 3	Tratamiento de la fibrosis pulmonar idiopática
Swedish	Rekombinant human monoklonal antikropp mot transformerande tillväxtfaktor (TGF) beta1, 2 och 3	Behandling av idiopatisk lungfibros
Norwegian	Rekombinant humant monoklonalt antistoff mot transformerende vekstfaktor beta-1, 2 og 3	Behandling av idiopatisk lungefibrose
Icelandic	Raðbrigða, manna einstofna mótefni gegn umbreytingar vaxtar þætti beta 1, 2 og 3	Meðferð sjálfvakinnar bandvefsmyndunar í lungum