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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in November 2005 on request of the sponsor.

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF human engineered monoclonal antibody specific for transforming growth factor ß1 (TGF- ß1) for the treatment of systemic sclerosis

On 4 February 2002, orphan designation (EU/3/01/080) was granted by the European Commission to Genzyme Europe BV, The Netherlands, for human engineered monoclonal antibody specific for Transforming Growth Factor ß1 for the treatment of systemic sclerosis.

What is systemic sclerosis?
Systemic sclerosis (also called scleroderma) is a disease of unknown cause, characterized by fibrosis of various severity in different organs such as the skin, blood vessels, digestive tract, lungs, heart and kidneys.

The condition is chronically debilitating and life threatening, in particular due to lung and kidney damage. Administration of a class of medicinal products called angiotensin-enzyme inhibitors is efficacious in preventing and treating severe renal complications. However, the progressive deterioration of the lung function remains life-threatening.

What are the methods of treatment available?
Several products with anti-inflammatory activity had been authorised for the condition in some countries in the Community at the time of submission of the application for orphan drug designation. Other products are also authorised in some countries in the Community for the treatment of high blood pressure in the lung vessels (pulmonary hypertension), which is one of the major causes for concern in systemic sclerosis.

The proposed antibody specific for TGF-β1 inhibits the action of TGF-β1. TGF-β1 appears to be involved in the production of connective tissue (fibrosis) and in the injury to the blood vessels and therefore the product has the potential to be developed as a causal treatment for the condition. Although efficacy evidence from systemic administration to humans is not available, the sponsor submitted satisfactory argumentation to assume that the product might be of potential significant benefit to the patients based on the described results in preclinical models of skin and organ fibrosis.

What is the estimated number of patients affected by the condition*?
According to the information provided by the sponsor, systemic sclerosis was considered to affect between 11,000 and 49,000 persons in the European Union.

How is this medicinal product expected to act?

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The active substance in the medicinal product is an antibody, which targets the TGF-ß1 and results in an inhibition of the action of this growth hormone.

What is the stage of development of this medicinal product?
At the time of the submission of the orphan drug designation application the effects of the product had been studied in experimental models of the condition. In addition first studies in humans were performed to investigate the safety of the product, but there were no data regarding potential efficacy.

This product had not been marketed or designated as orphan medicinal product elsewhere, 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 21 November 2001 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 be affecting 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 have been 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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*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001). This estimate is based on available information and calculations presented by the sponsor at the time of the application and may thus differ from the true number of patients affected by the condition.