



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

Document Date: London, 1 July 2005
Doc.Ref.: EMEA/COMP/85958/2005

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF

humanised agonistic anti-CD28 monoclonal antibody for the treatment of B-cell chronic lymphocytic leukemia

On 11 April 2005, orphan designation (EU/3/05/276) was granted by the European Commission to TeGenero AG, Germany, for humanised agonistic anti-CD28 monoclonal antibody for the treatment of B-cell chronic lymphocytic leukemia.

What is B-cell chronic lymphocytic leukemia?

B-cell chronic lymphocytic leukemia is a disease in which cancer cells are found in the blood and the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called “blasts” that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. White blood cells fight infection. Platelets support blood clotting. When leukemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukemias. B-cell chronic lymphocytic leukemia is a cancer of the white blood cells called lymphocytes. The lymphocytes multiply too quickly and live too long, so there are too many of them circulating in the blood. These leukemic lymphocytes look normal, but they are not fully developed and do not work properly. Over a period of time these abnormal cells replace the normal white cells, red cells and platelets in the bone marrow. It is the most common type of leukemia. B-cell chronic lymphocytic leukemia mainly affects older people and is rare in people under the age of 40. B-cell chronic lymphocytic leukemia is chronically debilitating and life-threatening due to the severe prognosis and the poor long-term survival for high-risk patients.

What are the methods of treatment available?

Treatment for leukemia is complex and depends on a number of factors including the type of leukemia, the extent of the disease and whether the leukemia has been treated before. It also depends on the age, the symptoms, and the general health of the patient. Some people with B-cell chronic lymphocytic leukemia never have treatment if their illness is not causing any symptoms and is progressing only very slowly. Treatment is only started if and when the symptoms become troublesome. Current main treatment of B-cell chronic lymphocytic leukemia is chemotherapy (using drugs to kill cancer cells). Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.

Humanised agonistic anti-CD28 monoclonal antibody could be of potential significant benefit for the treatment of chronic lymphocytic leukemia because it may offer a new way of killing cancer cells. This 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*?

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According to the information provided by the sponsor, B-cell chronic lymphocytic leukemia was considered to affect about 124,000 persons in the European Union.

How is this medicinal product expected to act?

Antibodies are proteins in the body that target and link specific shapes (the so-called antigens) on the surface of, various cells. Humanised agonistic anti-CD28 monoclonal antibody is an antibody that is thought to bind a specific type of cells of the immune system called T lymphocytes. By binding these cells, it is thought that the antibody can stimulate them to attack and kill the cancer cells.

What is the stage of development of this medicinal product?

The evaluation of the effects of humanised agonistic anti-CD28 monoclonal antibody in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with B-cell chronic lymphocytic leukemia were initiated.

Humanised agonistic anti-CD28 monoclonal antibody was not marketed anywhere worldwide for B-cell chronic lymphocytic leukemia or designated as orphan medicinal product elsewhere for this condition, 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 3 March 2005 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.

For more information:

Sponsor's contact details:

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*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.

Patients' associations contact points:

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

Language	Active Ingredient	Indication
English	Humanized Agonistic Anti-CD28 Monoclonal Antibody	Treatment of B-cell Chronic Lymphocytic Leukaemia (B-CLL)
Czech	Humanizovaná monoklonální agonistická protilátka anti –CD 28	Léčba chronické lymfocytární leukemie typu B (B-CLL)
Danish	Humaiseret agonistisk Anti CD28 monoclonal antistof	Behandling af b-celle kronisk lymfocytisk leukæmi (B-CLL)
Dutch	Gehumaniseerd agonistisch anti-CD28 monoclonaal antilichaam	Behandeling van B-cel chronische lymfocyttaire leukemie (B-CLL)
Estonian	Inimese agonistlik anti-CD28 monoklonaalne antikeha	B-rakulise kroonilise lümfotsütaarse leukeemia (B-CLL) ravi
Finnish	Humanisoitu agonistinen anti-CD28 monoklonaalinen vasta-aine	Kroonisen, lymfosyyttisen B-solu leukemian (B-CLL) hoito
French	Anticorps monoclonal humanisé dirigé contre le récepteur CD28	Traitement de la leucémie lymphoïde chronique à cellules B (LCC-B)
German	Humanisierter agonistisch wirkender Anti-CD28 monoklonater Antikörper	Behandlung der chronischen lymphozytischen B-Zellen Leukämie (B-CLL)
Greek	Ανθρωποποιημένο μονοκλωνικό αντίσωμα αγωνιστικό anti- CD28	Θεραπεία χρόνιας λεμφοκυτταρικής λευχαιμίας β- κυττάρων (B-CLL)
Hungarian	CD 28 elleni humanizált monoklonális, agonista ellenanyag	B sejtes krónikus lymphoid leukaemia (B-CLL) kezelése
Italian	Anticorpo monoclonale umanizzato agonista anti CD-28	Trattamento de leucemia linfocitica cronica (LCC)
Latvian	Cilvēka agonistiska monoklonāla anti-CD28 antivielā	B šūnu hroniskas limfocītiskās leukēmijas (B-CLL) ārstēšana
Lithuanian	Humanizuotas agonistinis anti – CD28 monokloninis antikūnas	B ląstelių lėtinės limfocitinės leukemijos (B – LLL) gydymas
Polish	Humanizowane agonistyczne przeciw CD 28 monoklonalne przeciwciało	Leczenie przewlekłej białaczki limfatycznej (B-CLL)
Portuguese	Anticorpo monoclonal humanizado agonista anti-CD28	Tratamento de leucemia linfocítica crónica de células B (LCC-B)
Slovak	Ľudská agonistická monoklonálna protilátka Anti-CD 28	Liečba chronickej lymfatickej leukémie (B-CLL)
Slovenian	Humanizirano agonistično anti-CD28 monoklonsko protiteleso	Zdravljenje kronične limfatske levkemije (B-CLL)

Spanish	Anticuerpo agonista monoclonal humanizado dirigido contra el receptor CD28	Tratamiento de leucemia linfoide crónica de células B (LCC-B)
Swedish	Human agonistisk anti CD28 monoklonal antikropp	Behandling av B-cell kronisk lymfocytisk leukemi (B-KLL)
Norwegian	Humanisert agonistisk anti-CD28 monoklonalt antistoff	Behandling av kronisk lymfatisk B-celle leukemi (B-KLL)
Icelandic	Manna aðlagð agonistískt and-CD 28 einstofna mótefni	Meðferð á langvinnu B-frumu eitilfrumuhvítblæði (B-CLL)