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

Document Date: London, 15 September 2009
Doc.Ref.: EMEA/COMP/546613/2008 Rev.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 for the treatment of hairy cell leukaemia

On 5 December 2008, orphan designation (EU/3/08/592) was granted by the European Commission to Medimmune Limited, United Kingdom, for murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 for the treatment of hairy cell leukaemia.

What is hairy cell leukaemia?
Hairy cell leukaemia is a cancer of the blood, when too many B-lymphocytes (a type of white blood cell) are produced. The term 'hairy cell' refers to the hair-like projections that can be seen on the surface of the lymphocytes when they are examined under a microscope. In this disease, the cancerous cells build up in the blood, bone marrow and spleen. This can cause an enlarged spleen, anaemia (low red blood cell counts), leucopenia (low white blood cell counts), problems with blood clotting including bruising and bleeding, and repeated infections. Patients also have general symptoms such as weakness, weight loss and shortness of breath. Hairy cell leukaemia makes up 2% of all leukaemias. Hairy cell leukaemia is life-threatening. Patients with this disease have poor long-term survival.

What is the estimated number of patients affected by the condition?
At the time of designation, hairy cell leukaemia affected less than 1 in 10,000 people in the European Union (EU) [*]. This is below the threshold for orphan designation, which is 5 in 10,000 people, and is equivalent to a total of around 50,000 people. This estimate is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
Treatment for hairy cell leukaemia is complex and depends on a number of factors including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. Treatment is usually started when symptoms become troublesome: some people with hairy cell leukaemia never need treatment if they do not have any symptoms and the disease is progressing slowly. Currently, the main treatment is chemotherapy (using medicines to kill cancer cells). At the time of submission of the application for orphan drug designation, several medicines were authorised for the disease in the EU.
The sponsor has provided sufficient information to show that murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 might be of potential significant benefit for the treatment of hairy cell leukaemia, because it might act in a different way to other medicines. This assumption will have to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

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

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.europa.eu http://www.emea.europa.eu

How is this medicine expected to work?
Murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 is made up of an antibody attached to part of a toxin from the bacterium *Pseudomonas*. Antibodies are proteins that are able to recognise and attach to structures called antigens. The part of the antibody in this medicine recognises and attaches to an antigen called CD22 cell-surface receptor, which is found on the surface of cancerous cells in hairy cell leukaemia. After attaching itself to CD22, the antibody and the attached toxin are taken up into the cells, where the toxin is activated. The toxin then stops the cancerous cells from making new proteins, eventually killing them.

What is the stage of development of this medicine?
The effects of murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 have been evaluated in experimental models.
At the time of submission of the application for orphan designation, clinical trials in patients with hairy cell leukaemia were ongoing.
At the time of submission, murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38 was not authorised anywhere worldwide for hairy cell leukaemia or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 October 2008 recommending the granting of this 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 five in 10,000 people in the Community) or the 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.

For more information:
Sponsor's contact details:
MEDIMMUNE Limited
Milstein Building
Granta Park
Great Abington
Cambridgeshire CB21 6GH
United Kingdom
Telephone: +44 1223 471 471
Telefax: +44 1223 471 472
E-mail: info@medimmune.com

Patients' associations contact points:

Ligue Nationale Contre le Cancer
14 Rue Corvisart
75013 Paris
France
Telephone: +33 1 53 55 24 00
Telefax: +33 1 43 36 91 10
E-mail: ligue@ligue-cancer.net

Deutsche Krebshilfe e. V.
Buschstr. 32
53113 Bonn
Germany
Telephone: +49 2 287 29 900
Telefax: +49 2 287 29 90 11
E-mail: deutsche@krebshilfe.de

Leukaemia CARE
One Birch Court
Blackpole East
Worcester
Worcestershire WR3 8SG
United Kingdom
Telephone: +44 1905 755977 / +44 845 521 3456
24 hour CARE line 0800 169 6680 (UK residents only)
Telefax: +44 1905 755166
E-mail: info@leukaemiacare.org.uk

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

Language	Active Ingredient	Indication
English	Murine anti-CD22 antibody variable region fused to truncated *Pseudomonas* exotoxin 38	Treatment of hairy cell leukaemia
Bulgarian	Мише анти-CD22 антитяло, свързано на различни места с фрагменти от *Pseudomonas* екзотоксин 38	Лечение на левкемична ретикулоендотелиоза
Czech	Variabilní oblast myší protilátky proti CD22 fúzovaná s fragmentem exotoxinu 38 bakterie *Pseudomonas*	Léčba vlasatobuněčné (trichocelulární) leukémie
Danish	Murint antistof mod CD22, variabel region, fusioneret med trunkeret *Pseudomonas*-eksotoksin 38	Behandling af hårcelleleukæmi
Dutch	Murien anti-CD22 antilichaam variabel gebied, gefuseerd met getrunceerd *Pseudomonas* exotoxine 38	Behandeling van leukemische reticulo-endotheliose
Estonian	Lühendatud Pseudomonas'e eksotoksiin 38 külge ühendatud hiire anti-CD22 antikeha varieeruv piirkond	Karvrakulise leukeemia ravi
Finnish	Muriiniin anti-CD22:n vasta-aineen vaihtelevaan alueeseen fuusioitu katkaistu Pseudomonas-eksotoksiini 38	Karvasoluleukemian hoito
French	Fusion d'une région variable d'anticorps anti-CD22 murin et d'une exotoxine 38 tronquée de Pseudomonas	Traitement de la leucémie à tricholeucocytes
German	Mit einem deletierten Pseudomonas Exotoxin 38 fusionierte variable Region des murinen Anti-CD22-Antikörpers	Behandlung der Haarzellenleukämie
Greek	Μεταβλητή περιοχή αντισωμάτων τρωκτικών anti-CD22 συγχωνευμένη με περικομμένη εξωτοξίνη ψευδομονάδας 38	Θεραπεία Τριχωτής Κυτταρικής Λευχαιμίας
Hungarian	Csonka *Pseudomonas* exotoxin 38 toxinhoz fuzionált egér anti-CD22 antitest variábilis régió	Hajas-sejtes leukémia kezelése
Italian	Regione variabile di anticorpo anti-CD22 murino, fusa con esotossina 38 troncata di Pseudomonas	Trattamento della leucemia a cellule capellute
Latvian	Peles antivielas pret CD-22 mainīgā daļa pievienota pie saīsinātā pseidomonas eksotoksīna 38	Mataino šūnu leikēmijas ārstēšana
Lithuanian	Kintama pelių anti-CD22 antikūno sritis sujungta su sutrumpintu Pseudomonas egzotoksinu 38	Plaukuotųjų ląstelių leukemijos gydymas
Maltese	Reġjun varjabbli ta' l-antikorp tal-ġrieden kontra CD22 magħqud ma' esotossina 38 maqtugħa tal-Pseudomonas	Kura tal-lewkimja ta' ċelluli muxgħarin
Polish	Mysie przeciwciało CD-22 z różnym	Leczenie białaczki

	regionem połączone ze skróconą Pseudomonas egzotoksyną 38	włochatokomórkowej
Portuguese	Fusão entre a região variável de anticorpos anti-CD22 de murino e uma forma truncada de exotoxina 38 de Pseudomonas	Tratamento de Leucemia das células pilosas (Tricoleucemia)
Romanian	Regiunea variabilă a anticorpului murin anti-CD22 fuzionată cu o formă trunchiată a exotoxinei 38 a Pseudomonas	Tratamentul leucemiei cu celule păroase
Slovak	Variabilná oblasť myšej protilátky proti CD 22 fúzovaná s fragmentom exotoxínu 38 baktérie Pseudomonas	Liečba vlasatobunkovej leukémie
Slovenian	Variabilno območje mišjega protitelesa za antigen CD22, spojeno s skrajšanim eksotoksinom 38 bakterij Psevdomonas	Zdravljenje dlakastocelične levkemije
Spanish	Región variable del anticuerpo murino anti-CD22 fusionada a la exotoxina 38 truncada de Pseudomonas	Tratamiento de la leucemia de células peludas
Swedish	Murin anti-CD22-antikropp, variabel region, förenad med trunkerat Pseudomonas exotoxin 38	Behandling av hårcellsleukemi
Norwegian	Murint antistoff mot CD22, variabel region, forent med trunkert pseudomonas-eksotoksin 38	Behandling av hårcelleleukemi
Icelandic	Músa nd-CD22 mótefni tengt breytilegu svæði við stýft Pseudomonas extotoxin 38	Meðferð Hairy Cell Leukaemia („hárfrumu“ hvítblæði)