



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

**Document Date:** London, 24 June 2009  
**Doc.Ref.:** EMEA/COMP/568150/2008

## **Committee for Orphan Medicinal Products**

### **Public summary of positive opinion for orphan designation of**

### **N2'-Deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody for the treatment of multiple myeloma**

On 3 December 2008, orphan designation (EU/3/08/593) was granted by the European Commission to Biotest AG, Germany, for N2'-Deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody for the treatment of multiple myeloma.

#### **What is multiple myeloma?**

Multiple myeloma is a cancer of a type of white blood cell called plasma cells. Plasma cells are found in the bone marrow, the spongy tissue inside the large bones in the body. In multiple myeloma the division of plasma cells becomes out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. This interferes with production of normal white blood cells, red blood cells and platelets (components that help the blood to clot), leading to complications such as anaemia (low red blood cell counts), bone pain and fractures, raised blood calcium levels and kidney disease. Multiple myeloma is a life-threatening disease.

#### **What is the estimated number of patients affected by multiple myeloma?**

At the time of designation, multiple myeloma affected approximately 2.2 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 111,000 people. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

#### **What treatments are available?**

At the time of submission of the application for orphan designation, several medicines were already authorised for multiple myeloma in the EU. The main treatment for multiple myeloma is chemotherapy (medicines to treat cancer) usually combined with steroids (medicines used to reduce the activity of the immune system). Treatment with radiotherapy (using radiation to kill cancer cells) can be very useful in treating pain and weakened bones. Interferon alfa, a protein normally produced by the body during viral infections, can sometimes be used in combination with chemotherapy. N2'-Deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody could be of potential significant benefit for the treatment of multiple myeloma because it works in a different way to other medicines and could be more selective for multiple myeloma. This assumption will need 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).

**How is this medicine expected to work?**

N2'-Deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody is made up of two components:

- a monoclonal antibody (a type of protein) that has been designed to recognise and bind to a specific structure called CD138. CD138 is a protein that is found on the surface of multiple myeloma cells, which helps the cells stick to each other and to the extracellular matrix (the framework of fibres surrounding the cells that provides support for their growth) as they enter the bone marrow;
- maytansine, a substance that kills cancer cells by interfering with their division.

The medicine is expected to bind to multiple myeloma cells via its monoclonal antibody part. Once on the cells, maytansine is expected to act locally and stop any further cell division. Through this mechanism, the medicine might lead to the death of multiple myeloma cells.

**What is the stage of development of this medicine?**

The effects of N2'-deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody have been evaluated in experimental models

At the time of submission of the application for orphan designation, no clinical trials in patients with multiple myeloma had been started.

At the time of submission, N2'-deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal antibody was not authorised anywhere in the world for multiple myeloma 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;
- and 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

**For more information:**

Sponsor's contact details:

Biotest AG

Landsteinerstrasse 5

D-63303 Dreieich

Germany

Telephone: +49 61 03 80 10

Telefax: +49 61 03 80 11 80

E-mail: [sibylle\\_kaiser@biotest.de](mailto:sibylle_kaiser@biotest.de)

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](mailto:ligue@ligue-cancer.net)

**Macmillan Cancer Support (merged with CancerBACUP)**

3 Bath Place

Rivington Street

London

EC2A 3JR

United Kingdom

Telephone: +44 20 7696 9003

Switchboard open during office hours, Mon–Fri, 9am–Noon and 2pm–4.45pm

Telefax: +44 20 7696 9002

**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](mailto:deutsche@krebshilfe.de)

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

| Language   | Active ingredient                                                                                                                                | Indication                             |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| English    | N2'-Deacetyl-N2'-[4-methyl-4-(oxobutylidithio)-1-oxopentyl]-maytansine-chimerised anti-CD138 IgG4 Monoclonal Antibody                            | Treatment of multiple myeloma          |
| Bulgarian  | Моноклонално химеризирано N2'-деацетил-N2'-[4-метил-4-(оксобутилдитио)-1-оксопентил]-майтанзин анти-CD138 IgG4 антитяло                          | Лечение на мултиплен миелом            |
| Czech      | Monoklonální, chimérická N2'-Deacetyl-N2'-[4-methyl-4-(oxobutylidithio)-1-oxopentyl]-maytansin anti-CD138 IgG4 protilátka                        | Léčba mnohočetného myelomu             |
| Danish     | Kimært, monoklonalt N2'-Deacetyl-N2'-[4-methyl-4-(oxobutylidithio)-1-oxopentyl]-maytansin- anti-CD138 IgG4 antistof                              | Behandling af multipelt myelom         |
| Dutch      | Chimere monoklonale anti-CD138-antilichamen klasse IgG4, geconjugeerd met N2'-deacetyl-N2'-[4-methyl-4-(oxobutylidithio)-1-oxopentyl]-maytansine | Behandeling van multipel myeloom       |
| Estonian   | N2'-deatsetüül-N2'-[4-metüül-4-(oksobutüülditio)-1-oksopentüül]-maitansiin kimäärne CD138-vastane IgG4 monoklonaalne antikeha                    | Multiibelse müeloomi ravi              |
| Finnish    | N2'-deasetyyli-N2'-[4-metyyli-4-(oksobutyyliditio)-1-oksopentyyli]-maitansiini kimeerinen anti-CD138 IgG4 – monoklonaalinen vasta-aine           | Multippeli myelooman hoito             |
| French     | Anticorps chimérique monoclonal IgG4 anti-CD138 N2'-désacétyl-N2'-[4-méthyl-4-(oxobutylidithio)-1-oxopentyl]-maytansine                          | Traitement du myélome multiple         |
| German     | Monoklonaler, chimärer N2'-Deacetyl-N2'-[4-methyl-4-(oxobutylidithio)-1-oxopentyl]-Maytansin anti-CD138 IgG4 Antikörper                          | Behandlung des multiplen Myeloms       |
| Greek      | Μονοκλωνικό, χημairικό αντίσωμα N2'-δεακετυλ-N2'-[4-μεθυλ-4-(οξοβουτυλδιθειο)-1-οξοπεντυλ]-μαϊτανσίνη αντι-CD138 IgG4                            | Θεραπευτική αγωγή πολλαπλού μυελώματος |
| Hungarian  | Monoklonális, kimérikus N2'-deacetil-N2'-[4-metil-4-(oxobutilditio)-1-oxopentil]-maitanzin anti-CD138 IgG4 antitest                              | Myeloma multiplex kezelése             |
| Italian    | Anticorpo monoclonale anti-CD138 di tipo IgG4 chimerizzato con N2'-deacetil-N2'-[4-metil-4-(ossobutilditio)-1-ossopentil]-maitansina             | Trattamento del mieloma multiplo       |
| Latvian    | N2'-deacetil-N2'-[4-metil-4-(oksobutilditio)-1-oksopentil]-maitansīna himerizētas IgG4 monoklonālās antivielas pret CD138                        | Multiplās mielomas ārstēšana           |
| Lithuanian | N2'-deacetil-N2'-[4-metil-4-(oksobutilditio)-1-oksopentil]-maitanzino chimerizuotas monokloninis antikūnis prieš CD138 IgG4                      | Dauginės mielomos gydymas              |
| Maltese    | Antikorp monoklonali kontra CD138 tat-tip IgG4 kimerizzat ma' N2'-deacetyl-N2'-[4-                                                               | Kura tal-mjeloma multipla              |

|            |                                                                                                                                    |                                  |
|------------|------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
|            | methyl-4-(oxobutylthio)-1-oxopentyl]-maytansine                                                                                    |                                  |
| Polish     | Chimeryczne przeciwciało monoklonalne anty-CD138 IgG4 z N2'-deacetylo-N2'-[4-metylo-4-(oksobutyloditio)-1-oksopentylo]-majtanzynem | Leczenie szpiczaka mnogiego      |
| Portuguese | Anticorpo monoclonal quimérico IgG4 anti-CD138 - N2'-desacetil-N2'-[4-metil-4-(oxobutilditio)-1-oxopentil]-maitansina              | Tratamento do mieloma múltiplo   |
| Romanian   | Anticorp monoclonal IgG4 anti-CD138 chimerizat cu N2'-deacetil-N2'-[4-metil-4-(oxobutilditio)-1-oxopentil]-maitansină              | Tratamentul mielomului multiplu  |
| Slovak     | N2'-deacetyl-N2'-[4-metyl-4-(oxobutylthio)-1-oxopentyl]-maytanzín-chimérizovaná anti-CD138 IgG4 monoklonálna protilátka            | Liečba mnohopočetného myelómu    |
| Slovenian  | N2'-deacetil-N2'-[4-metil-4-(oksobutildicio)-1-oksopentil]-maitanzin-himerno proti-CD138 IgG4 monoklonalno protitel                | Zdravljenje multiplega mieloma   |
| Spanish    | Anticuerpo monoclonal IgG4 anti-CD138 quimerizado N2'-desacetil-N2'-[4-metil-4-(oxobutilditio)-1-oxopentil]-maitansina             | Tratamiento del mieloma múltiple |
| Swedish    | Chimär monoklonal N2'-deacetyl-N2'-[4-metyl-4-(oxobutylthio)-1-oxopentyl]-maytansin IgG4-antikropp riktad mot CD138                | Behandling av multipelt myelom   |
| Norwegian  | Kimært, monoklonalt N2'-deacetyl-N2'-[4-metyl-4-(oxobutylthio)-1-oxopentyl]-maytansin IgG4-antistoff mot CD138                     | Behandling av myelomatose        |
| Icelandic  | N2'-Desetýl-N2'-[4-metýl-4-(oxóbútýldithíó)-1-oxópentýl]-maytansín-blendings einstofna mótefni gegn CD138 IgG4                     | Meðferð við mergfrumuæxli        |