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 NGR-human tumour necrosis factor for the treatment of malignant mesothelioma

On 3 June 2008, orphan designation (EU/3/08/549) was granted by the European Commission to MolMed S.p.A, Italy, for NGR-human Tumour Necrosis Factor for the treatment of malignant mesothelioma.

What is malignant mesothelioma?

Malignant mesothelioma is a cancer of the membrane that surrounds the lungs (the pleura) or, less commonly, of the membrane that lines the abdomen (the peritoneum). 'Malignant' means that the cancer is likely to spread easily to other parts of the body. Mesothelioma is a very rare disease, but has become more frequent over the last few decades. It is seen more often in men than women. Although it can occur at any time of life, it usually appears at an age of around 60 years.
The major cause of mesothelioma is thought to be exposure to asbestos. Approximately eight out of ten people with mesothelioma have been exposed to asbestos in the past, typically 30 to 40 years before the cancer develops.
Malignant mesothelioma is a life-threatening disease.

What treatments are available?

The most effective treatment for mesothelioma is the surgical removal of the tumour. However, this is not always possible because the tumour has often already spread to other parts of the body by the time it is diagnosed. The current standard treatment for malignant mesothelioma is pemetrexed, used in combination with cisplatin.
NGR-human tumour necrosis factor might be of potential significant benefit in the treatment of malignant mesothelioma because it has a novel mechanism of action. This assumption will need to be confirmed at the time of a marketing authorisation, to maintain the orphan status of the medicine.

What is the estimated number of patients affected by malignant mesothelioma*?

Based on the information provided by the sponsor and previous knowledge of the Committee, malignant mesothelioma was considered to affect approximately 0.5 in 10,000 people in the European Union, which, at the time of designation, corresponded to about 25,000 persons.

How is this medicine expected to act?

NGR-human tumour necrosis factor consists of two parts: NGR and human tumour necrosis factor:

- NGR is a protein that attaches to a receptor called CD13, which is found on the surface of the cells lining the new blood vessels that are formed around tumours;
- human tumour necrosis factor is a protein that can kill these cells.

* 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 502,282,135 (Eurostat 2008). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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Because it is attached to NGR, the cell-killing activity of tumour necrosis factor is concentrated at the cells lining the blood vessels formed around tumours. This combined effect results in damage to blood vessels supplying tumours, reducing its supply of oxygen and nutrients and leading to the tumour dying back.

What is the stage of development of this medicinal product?
At the time of submission of the application for orphan designation, no clinical trials were ongoing in patients with malignant mesothelioma.

At the time of submission, NGR-human tumour necrosis factor was not authorised anywhere in the world for malignant mesothelioma or designated as orphan medicinal product elsewhere for this condition.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 8 April 2008 a positive opinion recommending the granting 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 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 product's quality, safety and efficacy is necessary before it 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	NGR-human Tumour Necrosis Factor	Treatment of malignant mesothelioma
Bulgarian	NGR-човешки тумор некротизиращ фактор	Лечение на малигнен мезотелиом
Czech	NGR-lidský faktor nekrotizující nádory	Léčba maligního mezoteliomu
Danish	NGR human tumor nekrosefaktor	Behandling af malignt mesotheliom
Dutch	NGR-humaan tumornecrosefactor	Behandeling van maligne mesothelioom
Estonian	Inimese NRG tuumori nekroosi faktor	Pahaloomulise mesotelioomi ravi
Finnish	Ihmisen NGR-tuumorinekroositekijä	Malignin mesoteliooman hoito
French	NGR Facteur humain de nécrose tumorale	Traitement du mésothéliome malin
German	NGRhumaner Tumornekrosefaktor	Behandlung des malignen Mesothelioms
Greek	NGR-ανθρώπινος παράγοντας νέκρωσης όγκων	Θεραπεία κακοήθους μεσοθηλιώματος
Hungarian	NGR humán tumornekrózis faktor	Rosszindulatú mesothelioma kezelése
Italian	NGR-Fattore umano di necrosi tumorale	Trattamento del mesotelioma maligno
Latvian	NGR-cilvēka tumora nekrozes faktors	Ļaundabīgas mezoteliomas ārstēšana
Lithuanian	NGR-žmogaus navikų nekrozės faktorius	Piktybinės mezoteliomos gydymas
Maltese	NGR Fattur uman tan-nekrosi tat-tumur	Kura tal-mesoteljoma malinna
Polish	Sprzężony z NGR ludzki czynnik martwiczy nowotworu	Leczenie złośliwego międzybłoniaka
Portuguese	NGR-Factor de Necrose Tumoral Humano	Tratamento do Mesotelioma maligno
Romanian	NGR-Factor uman de necroză tumorală	Tratamentul mezoteliomului malign
Slovak	NGR-ľudský faktor nekrotizujúci nádory	Liečba malígneho mezoteliómu
Slovenian	NGR - tumorje nekrotizirajoči faktor pri ljudeh	Zdravljenje malignega mezotelioma
Spanish	NGR - Factor de necrosis tumoral humano	Tratamiento del mesotelioma maligno
Swedish	NGR-human tumörnekrosfaktor	Behandling av malignt mesoteliom
Norwegian	NGR-human tumornekrosefaktor	Behandling av malignt mesoteliom
Icelandic	Manna NGR-æxlisdrepsþáttur	Meðferð við illkynja miðþekjuæxli