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EMA/COMP/744278/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamine for the treatment of malignant mesothelioma

On 16 December 2014, orphan designation (EU/3/14/1391) was granted by the European Commission to TMC Pharma Services Ltd, United Kingdom, for 5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamine for the treatment of malignant mesothelioma.

What is malignant mesothelioma?

Malignant mesothelioma is a cancer that affects the mesothelial cells (found on the inner linings of the organs), mainly in the pleura (lining the lungs) and in the peritoneum (lining the abdominal cavity). It is usually caused by exposure to asbestos. Mesothelioma of the pleura causes difficulty breathing and chest pain, and mesothelioma of the peritoneum causes ascites (a build-up of fluid in the abdomen) and abdominal pain.

Malignant mesothelioma is life-threatening because it may lead to bowel obstruction, heart or breathing problems and lung infections. Survival is poor, with patients only living, on average, for a year after diagnosis.

What is the estimated number of patients affected by the condition?

At the time of designation, malignant mesothelioma affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. 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 designation, the main treatment for malignant mesothelioma was surgery followed by chemotherapy (medicines to treat cancer) or radiotherapy (treatment with radiation). If the disease

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

was too advanced for surgery, chemotherapy alone was used. Only one medicine, pemetrexed, was specifically authorised in the EU for the treatment of malignant mesothelioma.

The sponsor has provided sufficient information to show that 5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamine might be of significant benefit for patients with the condition. Studies in experimental models have shown improved effects of the medicine compared with a combination of pemetrexed and cisplatin (another cancer medicine). This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The medicine works by blocking the activity of 'mammalian target of rapamycin' (mTOR) and 'phosphoinositide-3-kinases' (PI3K), two types of enzymes involved in controlling cell growth. In many cancers including mesothelioma, the biological pathway involving mTOR and PI3K is overactive and enables the uncontrolled growth and spread of cancer cells. By blocking the actions of these enzymes, the medicine is expected to help slow down the growth and spread of the cancer.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

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

At the time of submission, the medicine was not authorised anywhere in the EU for malignant mesothelioma or designated as an 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 13 November 2014 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 5 in 10,000 people in the EU) or 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:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamine	Treatment of malignant mesothelioma
Bulgarian	5-[8-метил-9-(1-метилетил)-2-(4-морфолинил)-9H-пурин-6-ил]-2-пиримидинамин	Лечение на малигнен мезотелиом
Croatian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamin	Liječenje malignog mezotelioma
Czech	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamin	Léčba maligního mezoteliomu
Danish	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamin	Behandling af malignt mesotheliom
Dutch	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purine-6-yl]-2-pyrimidinamine	Behandeling van maligne mesotheliom
Estonian	5-[8-metüül-9-(1-metüületüül)-2-(4-morfolinüül)-9H-puriin-6-üül]-2-pürimidiinamiin	Pahaloomulise mesotelioomi ravi
Finnish	5-[8-metyyli-9-(1-metyyli-etyyli)-2-(4-morfolinyyli)-9H-puriini-6-yyli]-2-pyrimidiiniamiini	Malignin mesoteliooman hoito
French	5-[8-méthyl-9-(1-méthyléthyle)-2-(4-morpholinyl)-9H-purine-6-yl]-2-pyrimidinamine	Traitement du mésothéliome malin
German	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-Pyrimidinamin	Behandlung des malignen Mesothelioms
Greek	5-[8-μεθυλ-9-(1-μεθυλαιθυλ)-2-(4-μορφολινυλ)-9H-πουριν-6-υλ]-2-πυριμιδιναμίνη	Θεραπεία κακοήθους μεσοθηλιώματος
Hungarian	5-[8-metil-9-(1-metil-etil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamin	Malignus mesothelioma kezelése
Italian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamina	Trattamento del mesotelioma maligno
Latvian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purīn-6-il]-2-pirimidinamīns	Ļaundabīgas mezoteliomas ārstēšana
Lithuanian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinaminas	Piktybinės mezoteliomos gydymas
Maltese	5-[8-methyl-9-(1-methylethyl)-2-(4-morpholinyl)-9H-purin-6-yl]-2-pyrimidinamine	Kura tal-mesoteljoma malinna
Polish	5-[8-metylo-9-(1-metyloetylo)-2-(4-morfolinylo)-9H-puryno-6-ylo]-2-pirymidynamina	Leczenie złośliwego międzybłoniaka

¹ At the time of designation

Language	Active ingredient	Indication
Portuguese	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purina-6-il]-2-pirimidinamina	Tratamento do Mesotelioma maligno
Romanian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamină	Tratamentul mezoteliomului malign
Slovak	5-[8-metyl-9-(1-metyletyl)-2-(4-morfolinyl)-9H-purín-6-yl]-2-pyrimidínamin	Liečba malígneho mezoteliómu
Slovenian	5-[8-metil-9-(1-metiletil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamin	Zdravljenje malignega mezotelioma
Spanish	5-[8-metil-9-(1-metietil)-2-(4-morfolinil)-9H-purin-6-il]-2-pirimidinamina	Tratamiento del mesotelioma maligno
Swedish	5-[8-metyl-9-(1-metyletyl)-2-(4-morfolinyl)-9H-purin-6-yl]-2-pyrimidinamin	Behandling av malignt mesoteliom
Norwegian	5-[8-metyl-9-(1-metyletyl)-2-(4-morfolinyl)-9H-purin-6-yl]-2-pyrimidinamin	Behandling av malignt mesoteliom
Icelandic	5-[8-metýl-9-(1-metýletýl)-2-(4-morfólínýl)-9H-púrín-6-ýl]-2-pýrimidínamin	Meðferð við illkynja miðþekjuæxli