



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-methyl-4-({4-[(3-methyl(methylsulfonyl)aminopyrazin-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidin-2-yl)amino)benzamide hydrochloride for the treatment of malignant mesothelioma

On 7 June 2013, orphan designation (EU/3/13/1132) was granted by the European Commission to TMC Pharma Services Ltd, United Kingdom, for N-methyl-4-({4-[(3-methyl(methylsulfonyl)aminopyrazin-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidin-2-yl)amino)benzamide hydrochloride 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 (the lining of the lungs) and in the peritoneum (the lining of 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. Because the symptoms are not specific, the cancer is often detected at a late stage.

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

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

At the time of designation, malignant mesothelioma affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 25,000 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).

*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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).



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

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with malignant mesothelioma because early studies suggested it might reduce the number of cancer stem cells, which are thought to be a source of cancer cells and are also thought to encourage the spread of the disease and resistance to treatment. In addition, studies suggest that the medicine may be particularly beneficial to patients whose mesothelioma incorporates certain genetic mutations. These assumptions 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 blocks the action of certain enzymes, including the enzyme 'focal adhesion kinase' (FAK), which are involved in regulating cell function. In mesothelioma, these enzymes are overactive and promote the growth and spread of the cancer cells and the development of new blood vessels that supply the tumours. By blocking these enzymes, the medicine is expected to reduce 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, clinical trials with the medicine in patients with malignant mesothelioma were planned.

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 17 April 2013 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:

TMC Pharma Services Ltd
Lodge Farm Barn
Elvetham Park Estate, Fleet Road
Hartley Wintney
Hampshire RG27 8AS
United Kingdom
Telephone: +44 125 2842 255
Telefax: +44 125 2842 277
E-mail: info@tmconsultancy.com

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	N-methyl-4-({4-[(3-methyl(methylsulfonyl)aminopyrazin-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidin-2-yl)amino)benzamide hydrochloride	Treatment of malignant mesothelioma
Bulgarian	N-метил-4-({4-[(3-метил(метилсулфонил)амино]пиразин-2- ил}метил)амино]-5-(трифлуорометил)пиримидин-2-ил}амино)бензамид хидрохлорид	Лечение на малигнен мезотелиом
Czech	N-methyl-4-({4-[(3-methyl(methylsulfonyl)amino]pyrazin-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidin-2-yl)amino)benzamid-hydrochlorid	Léčba maligního mezoteliomu
Danish	N-methyl-4-({4-[(3-methyl(methylsulfonyl)amino]pyrazin-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidin-2-yl)amino)benzamid hydrochlorid	Behandling af malignt mesotheliom
Dutch	N-methyl-4-({4-[(3-methyl(methylsulfonyl)amino]pyrazine-2-yl)methyl]amino}-5-(trifluoromethyl)pyrimidine-2-yl)amino)benzamide-hydrochloride	Behandeling van maligne mesotheliom
Estonian	N-metüül-4-({4-[(3-metüül(metüülsulfonüül)amino]pürasiin-2-üül}metüül)amino]-5-(trifluorometüül)pürimidiin-2-üül}amino)bensamiidhüdrokloriid	Pahaloomulise mesotelioomi ravi
Finnish	N-metyyli-4-({4-[(3-metyyli(metyylsulfonyyli)amino]pyratsiini-2-yyli}metyyli)amino]-5-(trifluorometyyli)pyrimidiini-2-yyli}amino)bentsamidihydrokloridi	Malignin mesoteliooman hoito
French	Chlorhydrate de N-méthyl-4-({4-[(3-méthyl(méthylsulfonyl) amino]pyrazin-2-yl)méthyl]amino}-5-(trifluorométhyl)pyrimidin-2-yl)amino) benzamide	Traitement du mésothéliome malin
German	N-Methyl-4-({4-[(3-methyl(methylsulfonyl)amino]pyrazin-2-yl)methyl]amino}-5-(trifluormethyl) pyrimidin-2-yl)amino) benzamidhydrochlorid	Behandlung des malignen Mesothelioms
Greek	Υδροχλωρική Ν-μεθυλο-4-({4-[(3-μεθυλο(μεθυλοσουλφονυλ)αμινο]πυραζιν-2-υλο}μεθυλ)αμινο]-5-(τριφθορομεθυλο) πυριμιδινό-2-υλ}αμινο)βενζαμίδη	Θεραπεία κακοήθους μεσοθηλιώματος

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	N-metil-4-({4-[(3-metil(metil-szulfonil)amino]pirazin-2-il}metil)amino]-5-(trifluor-metil) pirimidin-2-il}amino)benzamid hidroklorid	Roszzindulatú mesothelioma kezelése
Italian	N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazin-2-il}metil)amino]-5-(trifluorometil) pirimidin-2-il}amino)benzamide cloridrato	Trattamento del mesotelioma maligno
Latvian	N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazīn-2-il}metil)amino]-5-(trifluormetil) pirimidīn-2-yl}amino)benzamīda hidrohlors	Ļaundabīgas mezoteliomas ārstēšana
Lithuanian	N-metil-4-({4-[(3-metil(metilsulfonil)aminopirazin-2-il}metil)amino]-5-(trifluorometil) pirimidin-2-il}amino)benzamido hidrochloridas	Piktybinės mezoteliomos gydymas
Maltese	N-methyl-4-({4-[(3-methyl(methylsulfonyl)aminopyrazin-2-yl}methyl)amino]-5-(trifluoromethyl)pyrimidin-2-yl}amino)benzamide hydrochloride	Kura tal-mesotelioma malinna
Polish	Chlorowodorek N-metylo-4-({4-[(3-metylo(metylsulfonylo) aminopirazylo-2-ylo}metylo)amino]-5-(trifluorometylo)pyrimidyno-2-ylo}amino)benzamidu	Leczenie złośliwego międzybłoniaka
Portuguese	N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazina-2-il}metil)amino]-5-(trifluorometil) pirimidina-2-il}amino)benzamida hidroclorito	Tratamento do Mesotelioma maligno
Romanian	Clorhidrat de N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazin-2-il}metil)amino]-5-(trifluorometil) pirimidin-2-il}amino)benzamidă	Tratamentul mezoteliomului malign
Slovak	N-metyl-4-({4-[(3-metyl(metylsulfonyl)amino]pyrazín-2-yl}metyl)amino]-5-(trifluorometyl) pyrimidín-2-yl}amino)benzamid-hydrochlorid	Liečba malígneho mezoteliómu
Slovenian	N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazin-2-yl}metil) amino]-5-(trifluorometil)pirimidin-2-il}amino)benzamid hidroklorid	Zdravljenje malignega mezotelioma
Spanish	Clorhidrato de N-metil-4-({4-[(3-metil(metilsulfonil)amino]pirazina-2-il}metil)amino]-5-(trifluorometil) piramidina-2-il}amino)benzamida	Tratamiento del mesotelioma maligno

Language	Active ingredient	Indication
Swedish	N-metyl-4-({4-[(3-metyl (metylsulfonyl)amino]pyrazin-2- yl}metyl)amino]-5-(trifluorometyl) pyrimidin-2-yl}amino)benzamid hydroklorid	Behandling av malignt mesoteliom
Norwegian	N-metyl-4-({4-[(3-metyl (metylsulfonyl)amino]pyrazin-2- yl}metyl)amino]-5-(trifluorometyl) pyrimidin-2- yl}amino)benzamidhydroklorid	Behandling av malignt mesoteliom
Icelandic	N-metýl-4-({4-[(3-metýl (metýlsúlfónýl)amínó]pýrazín-2- ýl}metýl)amínó]-5-(tríflúórómetyl) pýrimídín-2-ýl}amínó)benzamíð hýdróklóríð	Meðferð við illkynja miðþekjuæxli