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Public summary of opinion on orphan designation

N-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide methanesulfonate for the treatment of gastric cancer

On 27 February 2017, orphan designation (EU/3/17/1840) was granted by the European Commission to Sirius Regulatory Consulting Limited, United Kingdom, for N-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide methanesulfonate (also known as YN968D1 or apatinib mesylate) for the treatment of gastric cancer.

What is gastric cancer?

Gastric cancer is a cancer that starts in the stomach, generally in the glandular cells lining the inside of the stomach. It is often detected late because early signs of the disease are the same as those of less serious stomach conditions (such as heartburn, gas and excessive belching). At a later stage, gastric cancer causes unexplained weight loss, loss of appetite and general decline in health. Bleeding can occur, leading to anaemia (low red blood cell counts). Men are about twice as likely to develop the disease as women.

Gastric cancer is a serious and life-threatening illness that is associated with shortened life expectancy.

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

At the time of designation, gastric cancer affected approximately 3.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 196,000 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, some patients with gastric cancer were treated with surgery to remove part or the whole of the stomach. Chemotherapy (medicines to treat cancer) was generally used after surgery or on its own if surgery was not possible or the disease had spread to other parts of the body. Several chemotherapy medicines were authorised in the EU for use in gastric cancer, such as

^{*}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 515,700,000 (Eurostat 2017).

capecitabine, cisplatin, docetaxel, doxorubicin, epirubicin, fluorouracil, mitomycin, ramucirumab and trastuzumab. They were often used in combination.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with gastric cancer. Early studies have found that patients with gastric cancer that had spread to other parts of the body and in whom at least two previous treatments had not worked lived for longer without their disease getting worse and survived overall for longer when given this medicine. In addition, the medicine is given by mouth and may therefore be easier to take than available medicines given by injection. 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?

This medicine works by blocking some enzymes called tyrosine kinases that are found in 'vascular endothelial growth factor' (VEGF) receptors. These receptors, which can be found in high levels on the surface of cancer cells, are involved in the development of new blood vessels that supply the cancer. By blocking VEGF receptors, this medicine is expected to slow down the growth of cancer cells by reducing their blood supply.

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 gastric cancer were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for gastric cancer or designated as an orphan medicinal product elsewhere for this condition. The medicine had been authorised in China for gastric cancer.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 January 2017 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide methanesulfonate	Treatment of gastric cancer
Bulgarian	N-(4-(1-цианоциклопентил)фенил)-2-(4-пиридинил метил)амино-3-пиридинкарбоксами́д метансулфонат	Лечение на карцином на стомаха
Croatian	N-(4-(1-cijanociklopentil)fenil)-2-(4-piridinilmetil)amino-3-piridin karboksamid metansulfonat	Liječenje raka želuca
Czech	N-(4-(1-kyanocyklopentyl)fenyl)-2-(4-pyridinylmethyl)amino-3-pyridinkarboxamid-methansulfonát	Léčba karcinomu žaludku
Danish	N-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamid methansulfonat	Behandlingen af cancer ventriculi
Dutch	N-(4-(1-cyanocyclopentyl)fenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide-methaansulfonaat	Behandeling van maagkanker
Estonian	N-(4-(1-tsüanotsüklopentüül)fenüül)-2-(4-püridinüülmetüül)amino-3-püridiinkarboksamiid metaansulfonaat	Maovähi ravi
Finnish	N-(4-(1-syanosyklopentyyli)fenyyli)-2-(4-pyridinyylimetyyli)amino-3-pyridiini-karboksiamidimetaanisulfonaatti	Mahasyövän hoito
French	Méthanesulfonate de N-(4-(1-cyanocyclopentyl)phényl)-2-(4-pyridinylméthyl)amino-3-pyridinecarboxamide	Traitement du cancer gastrique
German	N-(4-(1-Cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamidmethansulfonat	Behandlung von Magenkarzinom
Greek	Μεθανοσουλφονικό N-(4-(1-κυανοκυκλοπεντυλ)φαινυλ)-2-(4-πυριδινυλμεθυλ)αμινο-3-πυριδινοκαρβοξαμίδιο	Θεραπεία του γαστρικού καρκίνου
Hungarian	N-(4-(1-ciano-ciklopentil)fenil)-2-(4-piridinil-metil)amino-3-piridin-karboxamid metánszulfonát	Gyomorrák kezelése
Italian	N-(4-(1-cianociclopentil)fenil)-2-(4-piridinilmetil)amino-3-piridinecarbrossamide metansulfonato	Trattamento del cancro gastrico
Latvian	N-(4-(1-ciānciklopentil)fenil)-2-(4-piridīnilmetil)amīn-3-piridīnkarboksamīda metānsulfonāts	Kuņģa vēža ārstēšana
Lithuanian	N-(4-(1-cianociklopentil)fenil)-2-(4-piridinilmetil)amino-3-piridinkarboksamido metansulfonatas	Skrandžio vėžio gydymas
Maltese	N-(4-(1-ċianoċiklopentil)fenil)-2-(4-piridinilmetil)amino-3-piridinekarboksamida metanesulfonat	Kura tal-kanċer gastriku
Polish	N-(4-(1-cyjanocyklopentylo)fenylo)-2-(4-pirydynylometylo)amino-3-pirydynokarboksamido metanosulfonian	Leczenie raka żołądka
Portuguese	Metanosulfonato de N-(4-(1-cianociclopentil)fenil)-2-(4-piridinil-metil)amino-3-piridinacarboxamida	Tratamento do carcinoma gástrico

¹ At the time of designation

Language	Active ingredient	Indication
Romanian	Metan-sulfonat de N-(4-(1-cianociclopentil)fenil)-2-(4-piridinilmetil)amino-3-piridin-carboxamidă	Tratamentul cancerului gastric
Slovak	Metánsulfonát N-(4-(1-kyanocyklopentyl)fenyl)-2-(4-pyridinylmetyl)amino-3-pyridínkarboxamidu	Liečba rakoviny žalúdka
Slovenian	N-(4-(1-cianociklopentil)fenil)-2-(4-piridinilmetil)amino-3-piridinkarboksamid metansulfonat	Zdravljenje karcinoma želodca
Spanish	Metanosulfonato de N-(4-(1-cianociclopentil)fenil)-2-(4-piridinilmetil)amino-3-piridincarboxamida	Tratamiento del cáncer de estómago
Swedish	N-(4-(1-cyanocyklopentyl)fenyl)-2-(4-pyridinylmetyl)amino-3-pyridinkarboxamid metansulfonat	Behandling av magcancer
Norwegian	N-(4-(1-cyanosyklopentyl)fenyl)-2-(4-pyridinylmetyl)amino-3-pyridinkarboksamidmetansulfonat	Behandling av magekreft
Icelandic	N-(4-(1-sýanósýklópentýl) fenýl)-2-(4-pýridínýlmetýl)amínó-3-pýridínkarboxamíð metansúlfónat	Meðferð við magakrabbameini