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Public summary of opinion on orphan designation

1-[4-Bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea for the treatment of gastrointestinal stromal tumours

On 12 October 2017, orphan designation (EU/3/17/1936) was granted by the European Commission to Worldwide Clinical Trials Limited, United Kingdom, for 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea (also known as DCC-2618) for the treatment of gastrointestinal stromal tumours.

What are gastrointestinal stromal tumours?

Gastrointestinal stromal tumours (GIST) are a group of cancers of the stomach and bowel called sarcomas, which are characterised by uncontrolled growth of cells in the supporting tissues of these organs. Symptoms include bleeding, anaemia (low red blood cell counts), tiredness, and abdominal (belly) pain and discomfort. GIST are most common in the stomach (60%), followed by the small intestine (30%), and then the colon and rectum (5%). GIST occur predominantly in middle-aged and older people, and are considered life threatening because the tumours could come back and also spread to other organs.

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

At the time of designation, GIST affected approximately 1.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 83,000 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, GIST were treated mainly by surgery to remove the tumour. The medicines imatinib, sunitinib and regorafenib were authorised in the EU for the treatment of GIST that had spread and could not be surgically removed.

*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).

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The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with GIST because data from early studies showed that it had a beneficial effect in patients whose tumour could not be treated with available medicines or had grown after such treatments. 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?

In GIST cells, two types of tyrosine kinase enzymes, KIT and PDGFRA, may be abnormal and overactive, which causes GIST cells to multiply out of control. The medicine stops these enzymes from working, including abnormal forms that cannot be blocked by other medicines. Giving the medicine by mouth is expected to stop GIST cells from multiplying and so slow down the growth of the tumours and reduce symptoms of the disease.

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 GIST were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for GIST. Orphan designation of the medicine had been granted in United States for GIST.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 October 2017 recommending the granting of this designation.

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea	Treatment of gastrointestinal stromal tumours
Bulgarian	1-[4-бромо-5-[1-етил-7-(метиламино)-2-оксо-1,2-дихидро-1,6-нафтиридин-3-ил]-2-флуорофенил]-3-фенилурея	Лечение на гастро-интестинални стромални тумори
Croatian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-okso-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-fenilurea	Liječenje gastrointestinalnih stromalnih tumora
Czech	1-[4-bromo-5-[1-etyl-7-(metylamino)-2-oxo-1,2-dihydro-1,6-naftyridin-3-yl]-2-fluorofenyl]-3-fenylurea	Léčba gastrointestinálních stromálních tumorů
Danish	1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea	Behandling af gastrointestinale stromale tumorer
Dutch	1-[4-broom-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naftyridin-3-yl]-2-fluorfenyl]-3-fenylureum	Behandeling van gastro-intestinale stromale tumoren
Estonian	1-[4-bromo-5-[1-etüül-7-(metüülamino)-2-okso-1,2-dihüdro-1,6-naftüridiin-3-üül]-2-fluorofenüül]-3-fenüüluurea	Seedetrakti stroomaalsete kasvajate ravi
Finnish	1-[4-bromi-5-[1-etyyli-7-(metyyliamino)-2-okso-1,2-dihydro-1,6-naftyridiini-3-yyli]-2-fluorofenyyli]-3-fenyyliurea	Ruuansulatuskanavan pahanlaatuisten stroomatuumorien hoito
French	1-[4-bromo-5-[1-éthyl-7-(méthylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophényl]-3-phénylurée	Traitement des tumeurs stromales gastrointestinales
German	1-[4-Brom-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorphenyl]-3-phenylharnstoff	Behandlung von gastrointestinalen Stromatumoren
Greek	1-[4-βρωμο-5-[1-αιθυλ-7-(μεθυλαμινο)-2-οξο-1,2-διυδρο-1,6-ναφθυριδιν-3-υλ]-2-φθοροφαινυλ]-3-φαινυλουρία	Θεραπεία των γαστρεντερικών στρωματικών όγκων
Hungarian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-oxo-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-fenylurea	Gasztrointesztinális stromalis tumorok kezelése
Italian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-oxo-1,2-diidro-1,6-naftiridin-3-yl]-2-fluorofenil]-3-fenilurea	Trattamento dei tumori stromali gastrointestinali
Latvian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-okso-1,2-dihidro-1,6-naftiridīn-3-il]-2-fluorfenil]-3-fenilurīnviela	Kuŋģa-zarnu trakta stromas audzēju terapija

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-okso-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3- fenilurėja	Skrandžio ir žarnų stromos auglių gydymas
Maltese	1-[4-bromo-5-[1-etil-7-(metilammino)-2-osso-1,2-diidro-1,6-naftiridin-3-il]-2-fluworofenil]-3-fenilurea	Kura ta' tumuri gastrointestinali li jiżviluppaw fit-tessuti konnettivi
Polish	1-[4-bromo-5-[1-etylo-7-(metyloamino)-2-okso-1,2-dihydro-1,6-naftyrydyno-3-ilo]-2-fluorofenylo]-3-fenylomocznik	Leczenie nowotworów podścieliska przewodu pokarmowego
Portuguese	1-[4-bromo-5-[1-etil-7-(metilamino)-2-oxo-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-fenilureia	Tratamento de tumores estromais gastrointestinais
Romanian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-oxo-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-feniluree	Tratamentul tumorilor stromale gastro-intestinale
Slovak	1-[4-bróm-5-[1-etyl-7-(metylamino)-2-oxo-1,2-dihydro-1,6-naftyridín-3-yl]-2-fluórfenyl]-3-fenylmočovina	Liečba gastrointestinálnych stromálnych nádorov
Slovenian	1-[4-bromo-5-[1-etil-7-(metilamino)-2-okso-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-fenilsečnina	Zdravljenje gastrointestinalnih stromalnih tumorjev
Spanish	1-[4-bromo-5-[1-etil-7-(metilamino)-2-oxo-1,2-dihidro-1,6-naftiridin-3-il]-2-fluorofenil]-3-fenilurea	Tratamiento de los tumores del estroma gastrointestinal
Swedish	1-[4-bromo-5-[1-etyl-7-(metylamino)-2-oxo-1,2-dihydro-1,6-naftyridin-3-yl]-2-fluorofenyl]-3-fenylurea	Behandling av gastrointestinala stromala tumörer
Norwegian	1-[4-brom-5-[1-etyl-7-(metylamino)-2-okso-1,2-dihydro-1,6-naftyridin-3-yl]-2-fluorfenyl]-3-fenylurea	Behandling av gastrointestinale stromale tumorer
Icelandic	1-[4-brómó-5-[1-etýl-7-(metýlamínó)-2-oxó-1,2-díhýdró-1,6-naftýridín-3-ýl]-2-flúorófenýl]-3-fenýlúrea	Meðferð við grunnfrumuæxlum í meltingarfærum