11 August 2017
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Public summary of opinion on orphan designation

(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine for the treatment of gastrointestinal stromal tumours

On 17 July 2017, orphan designation (EU/3/17/1889) was granted by the European Commission to PhaRA bvba, Belgium, for (S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine (also known as BLU-285) for the treatment of gastrointestinal stromal tumours.

What are gastrointestinal stromal tumours?

Gastrointestinal stromal tumours (GIST) belong to 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 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000 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, treatment of GIST mainly consisted in surgical removal of 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 did not respond to or had progressed after treatment with available medicines. 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?

This medicine belongs to a group of medicines called 'tyrosine kinase inhibitors', which block enzymes known as tyrosine kinases.

The medicine is expected to work in GIST by blocking the activity of tyrosine kinases found in receptors (targets) called 'KIT' and PDGFRα. These receptors are often abnormal (mutated) and overactive in GIST cells, causing them to multiply uncontrollably. By blocking these tyrosine kinases, the medicine is expected to help to slow down the growth of the tumour.

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 the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 June 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	(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine	Treatment of gastrointestinal stromal tumours
Bulgarian	(S)-1-(4-флуорофенил)-1-(2-(4-(6-(1-метил-1H-пиразол-4-ил)пироло[2,1-f][1,2,4]триазин-4-ил)пиперазин-ил)пиримидин-5-ил)етан-1-амин	Лечение на гастро-интестинални стромални тумори
Croatian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirolo[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etan-1-amin	Liječenje gastrointestinalnih stromalnih tumora
Czech	(S)-1-(4-fluorofenyl)-1-(2-(4-(6-(1-metyl-1H-pyrazol-4-yl)pyrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)etan-1-amin	Léčba gastrointestinálních stromálních tumorů
Danish	(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amin	Behandling af gastrointestinale stromale tumorer
Dutch	(S)-1-(4-fluorfenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine	Behandeling van gastro-intestinale stromale tumoren
Estonian	(S)-1-(4-fluorofenüül)-1-(2-(4-(6-(1-metüül-1H-pürasool-4-üül)pürrolo[2,1-f][1,2,4]triasiin-4-üül)piperasiin-üül)pürimidiin-5-üül)etaan-1-amiin	Seedetrakti stroomaalsete kasvajate ravi
Finnish	(S)-1-(4-fluorofenyyli)-1-(2-(4-(6-(1-metyyli-1H-pyratsoli-4-yl)pyrroli[2,1-f][1,2,4]triatsiini-4-yl)piperatsiini-yl)pyrimidiini-5-yl)etaani-1-amiini	Ruuansulatuskanavan pahanlaatuisten stroomatuumorien hoito
French	(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methel-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazine-4-yl)piperazine-yl)pyrimidine-5-yl)ethan-1-amine	Traitement des tumeurs stromales gastrointestinales
German	(S)-1-(4-Fluorphenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazinyl)pyrimidin-5-yl)ethan-1-amin	Behandlung von gastrointestinalen Stromatumoren
Greek	(S)-1-(4-φθοροφαινυλο)-1-(2-(4-(6-(1-μεθυλο-1H-πυραζολο-4-υλ)πυρρολο[2,1-f][1,2,4]τριαζιν-4-υλ)πιπεραζιν-υλ)πυριμιδινο-5-υλ)αιθανο-1-αμίνη	Θεραπεία των γαστρεντερικών στρωματικών όγκων
Hungarian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirrolo[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etán-1-amin	Gasztrointesztinális stromalis tumorok kezelése
Italian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazolo-4-il)pirrolo[2,1-f][1,2,4]triazina-4-il)piperazina-il)pirimidina-5-il)etan-1-ammina	Trattamento dei tumori stromali gastrointestinali
Latvian	(S)-1-(4-fluorfenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirolo[2,1-f][1,2,4]triazīn-4-il)piperazīn-il)pirimidīn-5-il)etān-1-amīns	Kuņģa-zarnu trakta stromas audzēju terapija

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirol[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etano-1-aminas	Skrandžio ir žarnų stromos auglių gydymas
Maltese	(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine	Kura ta' tumuri gastrointestinali li jiżviluppaw fit-tessuti konnettivi
Polish	(S)-1-(4-fluorofenylo)-1-(2-(4-(6-(1-metylo-1H-pirazolo-4-yl)pirolo[2,1-f][1,2,4]triazyno-4-yl)piperazyno-yl)pirymidyno-5-yl)etano-1-amina	Leczenie nowotworów podścieliska przewodu pokarmowego
Portuguese	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirrolo[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etan-1-amina	Tratamento de tumores estromais gastrointestinais
Romanian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirolo[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etan-1-amină	Tratamentul tumorilor stromale gastro-intestinale
Slovak	(S)-1-(4-fluórfenyl)-1-(2-(4-(6-(1-metyl-1H-pyrazol-4-yl)pyrolo[2,1-f][1,2,4]triazín-4-yl)piperazín-yl)pyrimidín-5-yl)etán-1-amín	Liečba gastrointestinálnych stromálnych nádorov
Slovenian	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirolo[2,1-f][1,2,4]triazin-4-il)piperazin-il)pirimidin-5-il)etan-1-amin	Zdravljenje gastrointestinalnih stromalnih tumorjev
Spanish	(S)-1-(4-fluorofenil)-1-(2-(4-(6-(1-metil-1H-pirazol-4-il)pirrolo[2,1-f][1,2,4]triazin-4-il)piperazin-l)pirimidin-5-il)etan-1-amina	Tratamiento de los tumores del estroma gastrointestinal
Swedish	(S)-1-(4-fluorofenyl)-1-(2-(4-(6-(1-metyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)etan-1-amin	Behandling av gastrointestinala stromala tumörer
Norwegian	(S)-1-(4-fluorfenyl)-1-(2-(4-(6-(1-metyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)etan-1-amin	Behandling av gastrointestinale stromale tumorer
Icelandic	(S)-1-(4-flúórófenýl)-1-(2-(4-(6-(1-metýl-1H-pýrasól-4-ýl)pýrróló[2,1-f][1,2,4]tríazín-4-ýl)píperasín-ýl)pýrimídín-5-ýl)etan-1-amín	Meðferð við grunnfrumuæxlum í meltingarfærum