



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide for the treatment of invasive aspergillosis

On 14 October 2016, orphan designation (EU/3/16/1738) was granted by the European Commission to F2G Ltd, United Kingdom, for 2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide (also known as F901318) for the treatment of invasive aspergillosis.

### What is invasive aspergillosis?

Invasive aspergillosis is an infection caused by species of fungi known as *Aspergillus*. Spores of these fungi are very widely present in the air, but normally do not cause disease. In some people, usually when the immune system (the body's natural defences) is weakened, the fungus can attack and invade the lungs and spread throughout the body via the bloodstream, damaging other organs and tissues including the heart, kidney, liver, brain, and bones.

Invasive aspergillosis is a life-threatening disease that can be fatal due to damage to the lungs and other organs.

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

At the time of designation, invasive aspergillosis affected approximately 1.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 87,000 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).

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\*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 513,700,000 (Eurostat 2016).



## What treatments are available?

At the time of designation, several antifungal medicines were authorised in the EU for the treatment of invasive aspergillosis, including amphotericin, caspofungin, isavuconazole, itraconazole, posaconazole and voriconazole.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with invasive aspergillosis, with laboratory studies showing that the medicine may be effective against infections resistant to azole antifungal 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 interferes with the production of pyrimidine, a compound the fungi need to make DNA. It does this by blocking an enzyme called dihydroorotate dehydrogenase (DHODH), which is involved in producing pyrimidine. The resulting lack of pyrimidine is expected to prevent the fungi from multiplying and spreading.

## 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 invasive aspergillosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for invasive aspergillosis 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 8 September 2016 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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Treatment of invasive aspergillosis
Bulgarian	2-(1,5-диметил-3-фенил-1Н-пирол-2-ил)-N-{4-[4-(5-флуоро-пиримидин-2-yl)пиперазин-1-ил]-фенил}-2-оксо-ацетамид	Лечение на инвазивна аспергилоза
Croatian	2-(1,5-dimetil-3-fenil-1H-pirol-2-yl)-N-{4-[4-(5-fluoro-pirimidin-2-yl)piperazin-1-il]-fenil}-2-okso-acetamide	Liječenje invazivne aspergiloze
Czech	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Léčba invazivní aspergilózy
Danish	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Behandling af invasiv aspergillose
Dutch	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Behandeling van invasieve aspergillose
Estonian	2-(1,5-dimetüü-3-fenüül-1H-pürrool-2-üül)-N-{4-[4-(5-fluoro-pürimidiin-2-üül)piperaziin-1-üül]-fenüü}-2-okso-atsetamiid	Invasiivse aspergilloosi ravi
Finnish	2-(1,5-dimetyyli-3-fenyyli-1H-pyrroli-2-yl)-N-{4-[4-(5-fluoro-pyrimidiini-2-yl)piperatsiini-1-yl]-fenyyli}-2-okso-asetamidi	Invasiivisen aspergilloosin hoito
French	2-(1,5-diméthyl-3-phényl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)pipérazin-1-yl]-phényl}-2-oxo-acétamide	Traitement des aspergilloses invasives
German	2-(1,5-Dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamid	Behandlung der invasiven Aspergillose
Greek	2-(1,5-διμεθυλ-3-φαινυλ-1Η-πυρρολ-2-yl)-N-{4-[4-(5-φλουορο-πυριμιδινη-2-yl)πιπεραζινη-1-yl]-φαινυλ}-2-οξο-ακεταμιδη	Θεραπεία της εν τω βάθει ασπεργίλλωσης
Hungarian	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamid	Invazív aspergillozis kezelése
Italian	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Trattamento dell'aspergillosi invasiva
Latvian	2-(1,5-dimetil-3-fenil-1H-pirol-2-il)-N-{4-[4-(5-fluoro-pirimidīn-2-il)piperazīn-1-il]-fenil}-2-okso-acetamīds	Invazīvas aspergilozes ārstēšana
Lithuanian	2-(1,5-dimetil-3-fenil-1H-pirol-2-il)-N-{4-[4-(5-fluor-pirimidin-2-il)piperazin-1-il]-fenil}-2-okso-acetamidās	Invazinės aspergiliozės gydymas

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Maltese	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Kura tal-aspergillosi li tinxtered mal-ġisem
Polish	2-(1,5-dimetylo-3-fenyl-1H-pirol-2-yl)-N-{4-[4-(5-fluoro-pyrimidyno-2-yl)piperazyn-1-yl]-fenyl}-2-okso-acetamid	Leczenie inwazyjnej aspergilozy
Portuguese	2-(1,5-dimetil-3-fenil-1H-pirrol-2-il)-N-{4-[4-(5-fluoropirimidin-2-il)piperazin-1-il]-fenil}-2-oxoacetamida	Tratamento da aspergilose invasiva
Romanian	2-(1,5-dimetil-3-fenil-1H-pirol-2-il)-N-{4-[4-(5-fluoro-pirimidin-2-il)piperazin-1-il]-fenil}-2-oxo-acetamidă	Tratamentul aspergilozei invazive
Slovak	2-(1,5-dimetyl-3-fenyl-1H-pyrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidín-2-yl)piperazín-1-yl]-fenyl}-2-oxo-acetamid	Liečba invazívnej aspergilózy
Slovenian	2-(1,5-dimetil-3-fenil-1H-pirol-2-il)-N-{4-[4-(5-fluoro-pyrimidin-2-il)piperazin-1-il]-fenil}-2-okso-acetamid	zdravljenje invazivne aspergiloze
Spanish	2-(1,5-dimethyl-3-fenil-1H-pirrol-2-il)-N-{4-[4-(5-fluoro-pirimidin-2-il)piperazin-1-il]-fenil}-2-oxo-acetamide	Tratamiento de aspergilosis invasiva
Swedish	2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Behandling av invasiv aspergillos
Norwegian	2-(1,5-dimetyl-3-fenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-fenyl}-2-okso-acetamid	Behandling av invasiv aspergillose
Icelandic	2-(1,5-dímetyl-3-phenýl-1H-pýrról-2-ýl)-N-{4-[4-(5-flúóró-pýrimídín-2-yl)píperazín-1-ýl]-phenýl}-2-oxó-acetamið	Meðferð á ífarandi aspergillosis