

19 May 2015  
EMA/COMP/211408/2015  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### 1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride for the treatment of cryptococcosis

On 24 April 2015, orphan designation (EU/3/15/1475) was granted by the European Commission to Arno Therapeutics UK, Limited, United Kingdom, for 1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride for the treatment of cryptococcosis.

#### What is cryptococcosis?

Cryptococcosis is an infection caused by one of two related kinds of fungus called *Cryptococcus neoformans* and *Cryptococcus gattii*. It is a type of unusual infection called an opportunistic infection. Opportunistic infections affect people whose immune system (the body's natural defences) is not working properly, including patients with AIDS due to poorly controlled HIV infection and those who are receiving medicines to suppress the immune system following a bone marrow or organ transplant. Cryptococcosis can lead to signs and symptoms affecting various parts of the body, including fever, rash, cough and chest pain due to lung infection and symptoms of meningitis (inflammation of the membranes around the brain), including headache, altered consciousness and problems with vision.

Cryptococcosis is a long-term debilitating and potentially life-threatening condition due to its effects on organs such as the lung and brain.

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

At the time of designation, cryptococcosis affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 26,000 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 512,900,000 (Eurostat 2015).

## **What treatments are available?**

At the time of application, several medicines for fungal infections were authorised in the EU for treatment of cryptococcosis, including amphotericin, flucytosine and fluconazole.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with cryptococcosis because it works in a different way to existing medicines and studies in experimental models suggest that it may improve the outcome of patients when added to existing treatment. 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?**

The medicine is thought to work by enhancing the ability of cells in the body to attack and destroy the fungus. In addition, the medicine is thought to block the action of certain enzymes in the fungus that the fungal cells need for their growth and survival. By blocking these enzymes, the medicine causes fungal cells to die or prevents them from spreading.

## **What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, the evaluation of the effects of this medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with cryptococcosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for cryptococcosis 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 19 March 2015 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:

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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	1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride	Treatment of cryptococcosis
Bulgarian	1-(4-(N-глицилами́до)фенил)-3-трифлуорометил-5-(фенантрен-2-ил)-пиразол-хидрохлорид	Лечение на криптококоза
Croatian	1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenantren-2-il)-pirazolklorid	Liječenje kriptokokoze
Czech	1-(4-(N-glycylamido)fenyl)-3-trifluormethyl-5-(fenantren-2-yl)pyrazol-hydrochlorid	Léčba kryptokokózy
Danish	1-(4-(N-glycylamido)phenyl)-3-trifluormethyl-5-(phenanthren-2-yl)pyrazol-hydrochlorid	Behandling af cryptokokkose
Dutch	1-(4-(N-glycylamido)fenyl)-3-trifluormethyl-5-(fenantreen-2-yl)pyrazool-hydrochloride	Behandeling van cryptococcosis
Estonian	1-(4-(N-glütsüülamido)fenüül)-3-trifluorometüül-5-(fenantreen-2-üül)pürasool-hüdrokloriid	Krüptokokkoosi ravi
Finnish	1-(4-(N-glysyylamido)fenyyli)-3-trifluorimetyyli-5-(fenantren-2-yyli)pyratsoli-hydrokloridi	Kryptokokkoosin hoito
French	Chlorhydrate de 1-(4-(N-glycylamide)phényl)-3-trifluorométhyl-5-(phénanthrén-2-yl)pyrazole	Traitement de la cryptococcose
German	1-(4-(N-glycylamido)phenyl)-3-trifluormethyl-5-(phenanthren-2-yl)-pyrazol-hydrochlorid	Behandlung der Kryptokokkose
Greek	1-(4-(N-γλυκυλάμιδο)φαινυλ)-3-τριφθορομεθυλ-5-(φαινανθρεν-2-υλ)πυραζολο-υδροχλωρίδιο	Θεραπεία της κρυπτοκόκκωσης
Hungarian	1-(4-(N-glicil)fenil)-3-trifluoro-5-(fenantren-2-il)-pirazol hidroklorid	Cryptococcosis kezelése
Italian	1-(4-(N-glycylamido)fenil)-3-trifluorometil-5-(phenanthren-2-il)-pirazolo-cloridrato	Trattamento della criptococcosi
Latvian	1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenanthrēn-2-il)pirazol-hidrohlorīds	Kriptokokozes ārstēšana
Lithuanian	1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenantren-2-il)-pirazolo-hidrochloridas	Kriptokokozės gydymas
Maltese	1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride	Kura tal-kriptokokkosi
Polish	1-(4-(N-glicyloamido)fenylo)-3-trifluorometylo-5-(fenantren-2-ylo)pirazol chlorowodorek	Leczenie kryptokokozy
Portuguese	Cloridrato de 1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenantren-2-il)-pirazol	Tratamento da criptococose
Romanian	Clorhidrat de 1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenantren-2-il)pirazol	Tratamentul criptococozei
Slovak	1-(4-(N-glycylamido)fenyl)-3-trifluórmetyl-5-(fenantren-2-yl)pyrazol-hydrochlorid	Liečba kryptokokózy

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

Language	Active ingredient	Indication
Slovenian	1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenanthren-2-il)pirazol-hidroklorid	Zdravljenje kriptokokoze
Spanish	Clorhidrato de 1-(4-(N-glycylamido)fenil)-3-trifluorometil-5-(fenantren-2-il)pirazol-	Tratamiento de la criptococosis
Swedish	1-(4-(N-gycylamido)fenyl)-3-trifluormetyl-5-(fenantren-2-yl)pyrazol-hydroklorid	Behandling av kryptokockos
Norwegian	1-(4-(N-glysylamido)fenyl)-3-trifluormetyl-5-(fenantren-2-yl)pyrazolhydroklorid	Behandling av kryptokokkose
Icelandic	1-(4-(N-glýkýlamídó)fenýl)-3-tríflúormetýl-5-(fenantren-2-ýl)pýrazól-hýdróklóríð	Meðferð cryptococcosis