

10 July 2018  
EMA/272912/2018

## Public summary of opinion on orphan designation

### Itraconazole for the prevention of invasive aspergillosis

On 25 May 2018, orphan designation (EU/3/18/2024) was granted by the European Commission to Galephar M/F, Belgium, for itraconazole for the prevention 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 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 at risk of developing the condition?

At the time of designation, the number of patients at risk of invasive aspergillosis was estimated to be less than 2 people in 10,000 in the European Union (EU). This was equivalent to a total of fewer than 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 methods of prevention are available?

At the time of designation, several antifungal medicines were used in the EU for the prevention of invasive aspergillosis, including amphotericin, caspofungin, isavuconazole, itraconazole, posaconazole, voriconazole. These medicines were mostly available for use by injection or by mouth.

The sponsor has provided sufficient information to show that the medicine (itraconazole by inhalation) might be of significant benefit for patients at risk of invasive aspergillosis. Laboratory data showed

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\*Disclaimer: For the purpose of the designation, the number of patients at risk of developing 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 517,400,000 (Eurostat 2018).

greater clearance of the infection and higher survival with the medicine given by inhalation than with another antifungal medicine given by mouth. In addition, the inhalation route may offer better safety.

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?**

Itraconazole has been used to treat fungal infections for several years. It works by blocking certain enzymes in the fungus known as cytochrome p450, thus preventing the formation of ergosterol, which is an important part of fungal cell walls. This ultimately leads to the fungus' death and clearance of the infection.

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

The effects of the itraconazole 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 at risk of invasive aspergillosis had started.

At the time of submission, itraconazole was not authorised anywhere in the EU for prevention of 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 19 April 2018 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	Itraconazole	Prevention of invasive aspergillosis
Bulgarian	Итраконазол	Лечение на инвазивна аспергилоза
Croatian	Itrakonazol	Prevenција invazivne aspergiloze
Czech	Itrakonazol	Prevence invazivní aspergilózy
Danish	Itraconazol	Forebyggelse af invasiv aspergillose
Dutch	Itraconazol	Preventie van invasieve aspergillose
Estonian	Itrakonasool	Invasiivse aspergilloosi ennetamine
Finnish	Itrakonatsoli	Invasiivisen aspergilloosin ehkäisy
French	Itraconazole	Prévention des aspergilloses invasives
German	Itraconazol	Prävention der invasiven Aspergillose
Greek	Ιτραконаζόλη	Πρόληψη της εν τω βάθει ασπεργίλλωσης
Hungarian	Itrakonazol	Invazív aspergillosis megelőzése
Italian	Itraconazolo	Prevenzione dell'aspergillosi invasiva
Latvian	Itrakonazols	Invazīvas aspergilozes ārstēšana
Lithuanian	Itrakonazolas	Invazinės aspergiliozės prevencija
Maltese	Itrakonazol	Prevenzjoni tal-aspergillozi li tinxtered mal-ġisem
Polish	Itrakonazol	Zapobieganie inwazyjnej aspergilozie
Portuguese	Itraconazol	Prevenção da aspergilose invasiva
Romanian	Itraconazol	Prevenția aspergilozei invazive
Slovak	Itrakonazol	Prevenčia invazívnej aspergilózy
Slovenian	Itrakonazol	Preprečevanje invazivne aspergiloze
Spanish	Itraconazol	Prevención de aspergilosis invasiva
Swedish	Itrakonazol	Förebyggande av invasiv aspergillos
Norwegian	Itrakonazol	Forebygging av invasiv aspergillose
Icelandic	Ítrakónazól	Forvörn gegn ífarandi aspergillosis

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