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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Amphotericin B (for inhalation use) for the prevention of pulmonary fungal infections in patients deemed at risk

First publication	1 April 2009
Rev.1: transfer of sponsorship	30 March 2011
Rev.2: transfer of sponsorship	1 October 2014

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 28 August 2006, orphan designation (EU/3/06/391) was granted by the European Commission to Nektar Therapeutics UK Ltd, United Kingdom, for amphotericin B (for inhalation use) for the prevention of pulmonary fungal infections in patients deemed at risk.

The sponsorship was transferred to Kendle International Ltd, United Kingdom, in August 2010 and subsequently to Novartis Europharm Limited, United Kingdom, in March 2014.

What is pulmonary fungal infection in patients deemed at risk?

Every day we inhale many sorts of particles that are present in the environment, including spores, which are single dormant fungal cells. In healthy individuals these spores normally can't cause any harm because they are taken care of by our immune system (the body's natural defence system). In patients that for some reason have a weakened immune system (are immunosuppressed), however, these spores can become activated and the condition (colonisation) can develop into a lung fungal infection. There are several conditions that can cause immunosuppression including medicines that prevent transplanted organ rejection, blood cancers (leukaemias and lymphomas) and cancer treatments (chemotherapy), human immunodeficiency virus infection (HIV) and acquired immunodeficiency syndrome (AIDS). Symptoms of pulmonary fungal infection are shortness of breath, chest pain, cough, fever and weight loss. Pulmonary fungal infection is life-threatening due to the high risk of severe pulmonary disease and fungal sepsis (infection of the blood).

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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 developing pulmonary fungal infection was estimated to be approximately 2.2 people in 10,000 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 methods of prevention are available?

Currently the same medicinal products that are authorised for the treatment of pulmonary fungal infections, are also used for prevention including amphotericin B used intravenously. These products aim to kill the fungal cells through interfering with its cell membrane, the layer that surrounds and encapsulates the fungal cell.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that amphotericin B might be of potential significant benefit for the prevention of pulmonary fungal infection in patients deemed at risk, mainly because it may have less side effects than the product used intravenously. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Amphotericin B is a molecule that is designed to bind to substances called sterols. These are lipid structures found mainly in the outer membranes of cells. In humans the most abundant sterol is cholesterol and in fungal cells it is a related molecule called ergosterol. When amphotericin B binds to ergosterol it disrupts the ordered structure of the cell membrane and small holes (pores) are created. According to the sponsor, amphotericin B will kill the fungal cells by this mechanism and thus prevent them from colonising the lungs and causing an infection. Amphotericin B (for inhalation use) will only be delivered locally to the lungs.

What is the stage of development of this medicine?

The effects of amphotericin B (for inhalation use) were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients deemed at risk of developing pulmonary fungal infections were ongoing.

Amphotericin B (for inhalation use) was not authorised anywhere worldwide for the prevention of pulmonary fungal infections in patients deemed at risk, at the time of submission. Orphan designation of amphotericin B was granted in the United States for prevention of pulmonary fungal infections in patients at risk for aspergillosis due to immunosuppressive therapy including those receiving organ or stem cell transplants, or treated with chemotherapy or radiation for haematologic malignancies.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 July 2006 recommending the granting of this designation.

*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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 468,900,000 (Eurostat 2006).

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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Amphotericin B (inhalation use)	Prevention of pulmonary fungal infection in patients deemed at risk
Bulgarian	Amfotericín B (inhalačné použitie)	Prevencia mykotickej infekcie pľúc u rizikových pacientov
Croatian	Amfotericin B (za primjenu u dišne putove)	Prevencija gljivične infekcije pluća u bolesnika pod rizikom
Czech	Amfotericin B (za inhaliranje)	Preprečevanje glivičnih okužb pljuč pri bolnikih z domnevnim tveganjem zanje
Danish	Anfotericina B (via inhalatoria)	Prevención de la infección pulmonar por hongos en pacientes de riesgo
Dutch	Amfotericin B (användning för inhalation)	Förebyggande av pulmonella svampinfektioner, hos riskpatienter
Estonian	Amfotericin B (bruk til inhalasjon)	Forebygging av pulmonal soppinfeksjon hos pasienter når slik risiko foreligger
Finnish	Amfóterisín B (til innöndunar)	Til að koma veg fyrir sveppa lungnasýkingar hjá sjúklingum sem teljast í aukinni áhættu
French	Amphotéricine B (voie inhalée)	Prévention des infections fongiques pulmonaires chez les patients à risque
German	Amphothericin B (zur Inhalation)	Prävention pulmonaler Pilzinfektionen bei Risikopatienten
Greek	Αμφοτερικίνη Β (εισπνεόμενη)	Πρόληψη των πνευμονικών μυκητιασικών λοιμώξεων σε ασθενείς υψηλού κινδύνου
Hungarian	Amphotericin B (inhalációs alkalmazás)	Tüdő gombás fertőzésének prevenciója veszélyeztetett betegeknél
Italian	Amfotericina B (uso inalatorio)	Prevenzione delle infezioni polmonari fungine in pazienti ritenuti a rischio
Latvian	Amfotericīns B (inhalācijai)	Plaušu sēnīšu infekcijas profilakse riskam pakļautiem slimniekiem
Lithuanian	Amfotericinas B (inhaliuoti)	Plaučių grybelinės infekcijos, pacientams su galima rizika, prevencija
Maltese	Amphotericin B (għal biex jingibed man-nifs)	Prevenzjoni ta' infezzjonijiet fungali fil-pulmun f'pazjenti kkunsidrati f'riskju
Polish	Amfoterycyna B (podanie wziewne)	Zapobieganie zakażeniom grzybiczym płuc u pacjentów z grupy ryzyka
Portuguese	Anfotericina B (via inalatoria)	Prevenção de infecção pulmonar fúngica em doentes de risco
Romanian	Amfotericina B (pentru uz inhalator)	Prevenirea infectiilor fungice pulmonare la pacientii considerati la risc
Slovak	Amfotericín B (inhalačné použitie)	Prevencia mykotickej infekcie pľúc u rizikových pacientov
Slovenian	Amfotericin B (za inhaliranje)	Preprečevanje glivičnih okužb pljuč pri bolnikih z domnevnim tveganjem zanje

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Spanish	Anfotericina B (via inhalatoria)	Prevención de la infección pulmonar por hongos en pacientes de riesgo
Swedish	Amfotericin B (användning för inhalation)	Förebyggande av pulmonella svampinfektioner, hos riskpatienter
Norwegian	Amfotericin B (bruk til inhalasjon)	Forebygging av pulmonal soppinfeksjon hos pasienter når slik risiko foreligger
Icelandic	Amfóterisín B (til innöndunar)	Til að koma veg fyrir sveppa lungnasýkingar hjá sjúklingum sem teljast í aukinni áhættu