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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human monoclonal antibody to hsp90 for the treatment of invasive fungal infections

First publication	12 March 2009
Rev.1: administrative update	4 May 2011
Rev.2: withdrawal from the Community Register	8 November 2011
Rev.3: sponsor's change of address	5 February 2015

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.

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in September 2011 on request of the Sponsor.

On 5 December 2001, orphan designation (EU/3/01/073) was granted by the European Commission to NeuTec Pharma plc, United Kingdom, for recombinant human monoclonal antibody to hsp90 for the treatment of invasive fungal infections.

The sponsorship was transferred to Novartis Europharm Limited, in June 2007.

What is invasive fungal infection?

Invasive fungal infections are serious infections from various types of fungal species. The most common invasive fungal infections include invasive candidosis, aspergillosis, and cryptococcosis.

Invasive candidosis, also known as systemic candidosis or candidiasis, is an infection of visceral organs (large interior organs in the body cavities such as abdomen) by yeasts of the genus *Candida.* It encompasses infections that range from superficial to systemic. While superficial infections of skin and mucosal membranes, such as oral or vaginal thrush, cause local inflammation (redness and swelling) and discomfort, the systemic infections are potentially life threatening, especially in severely

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immunocompromised persons (immune system is not working properly) where the infection can spread through the blood stream to multiple organs.

Invasive aspergillosis is an acute infection caused by the micro-organism *Aspergillus*. This infection affects mainly patients with a weak immune system, including patients with AIDS or neutropenia (abnormally low number of a type of white blood cell called a neutrophil). A rapidly invasive aspergillus infection in the lungs often causes cough, fever, chest pain, and difficulty in breathing. Aspergillosis affecting the deeper tissues makes a person very ill. Symptoms include fever, chills, shock, and blood clots. Patients may develop kidney and liver failure.

Cryptococcosis is another serious and potentially fatal fungal disease which similar to other invasive fungal infections, affects mostly people with a defective immune system. Cryptococcosis is due to *Cryptococcous neoformas*. The symptoms include chest pain, dry cough, swelling of the abdomen, headache, blurred vision, and confusion. Invasive fungal infections are life threatening.

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

At the time of designation, invasive fungal infections affected 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 11,000 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?

Several anti-fungal medicinal products were authorised for the condition in the Community at the time of submission of the application for orphan designation.

Recombinant human monoclonal antibody to hsp90 might be of potential significant benefit for the treatment of invasive fungal infections, because it could improve the treatment of invasive fungal infections. 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?

Hsp90 is a protein synthesised by the microorganisms in response to stress. It is thought to play role in fungal infections. Recombinant human monoclonal antibody to hsp90 is made by a cell that has received a gene (DNA) that makes it able to produce a protein called hsp90 (heat shock protein 90). Antibodies are proteins naturally found in the blood that help the body to fight infections and other diseases. The recombinant human monoclonal antibody to hsp90 is expected to recognise the hsp90 produced by the fungi, and to bind to it, thus triggering the body's immune system to attack and lower levels of fungi causing infection.

What is the stage of development of this medicine?

The effects of recombinant human monoclonal antibody to hsp90 were evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial in patients with invasive fungal infections was ongoing.

[*]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.
At the time of designation, this represented a population of 378,800,000 (Eurostat 2001).

Recombinant human monoclonal antibody to hsp90 was not marketed anywhere worldwide for the treatment of invasive fungal infections or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 September 2001 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[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Recombinant human monoclonal antibody to hsp90	Treatment of invasive fungal infections
Bulgarian	Рекомбинантно човешко моноклонално антитяло към hsp90	Лечение на инвазивна гъбична инфекция
Czech	Rekombinantní lidská monoklonální protilátka k hsp 90	Léčba invazivní mykotické infekce
Danish	Humant rekombinant monoklonalt antistof overfor hsp90	Behandling af systemiske svampeinfektioner
Dutch	Recombinant humaan monoclonaal anti-hsp90 antilichaam	Behandeling van invasieve gist en schimmel infecties
Estonian	Rekombinantne inimese monoklonaalne antikeha hsp90 vastu	Invasiivse seeninfektsiooni ravi
Finnish	Rekombinantti humaani monoklooninen hsp90-vasta-aine	Invasiivisten sieni-infektioiden hoito
French	Anticorps monoclonal humain recombinant anti-hsp90	Traitement des infections fungiques systémiques
German	Humaner rekombinanter monoklonarer anti-hsp90 Antikörper	Behandlung von invasiven Pilzinfektionen
Greek	Ανασυνδυασμένο ανθρώπινο μονοκλωνικόαντίσωμα έναντι του hsp90	Θεραπεία των διεισδυτικών μυκητοειδών μολύνσεων
Hungarian	Hsp 90 ellenes rekombináns humán monoklonális ellenanyag	Invazív gombás fertőzések kezelése
Italian	Anticorpo umano recombinante monoclonale anti-hsp90	Trattamento di infezioni fungine invasive
Latvian	Rekombinanta cilvēka monoklonālā antiviela pret hsp 90	Invazīvo sēnīšu infekciju ārstēšana
Lithuanian	Žmogaus rekombinantinis monokloninis antikūnis prieš hsp90	Invazinių grybelinių infekcijų gydymas
Maltese	Anti-korp monoklonali uman rikombinanti għall-hsp90	Kura ta' infezzjonijiet fungali li jinxterdu mal-ġisem
Polish	Ludzkie rekombinowane przeciwciało monoklonalne przeciwko hsp 90	Leczenie inwazyjnej grzybicy
Portuguese	Anticorpo monoclonal humano recombinante anti-hsp90	Tratamento das infecçãoes fúngicas invasivas
Romanian	Anticorp monoclonal uman recombinant anti hsp90	Tratamentul infecţiilor fungice invazive.
Slovak	Rekombinantná ľudská protilátka voči hsp 90	Liečba invazívnych hubových infekcií
Slovenian	Rekombinantno humano protitelo proti hsp90	Zdravljenje invazivnih glivičnih okužb
Spanish	Anticuerpo monoclonal recombinante humano anti-hsp90	Tratamiento de infecciones fúngicas invasivas

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Swedish	Human genetisk rekombinant monoklonal antikropp till hsp 90	Behandling av systemiska svampinfektioner