6 February 2015
EMA/COMP/4684/2003 Rev.3
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Tobramycin (inhalation powder) for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis

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| First publication | 16 April 2003 |
| Rev.1: transfer of sponsorship | 6 March 2007 |
| Rev.2: information about Marketing Authorisation | 1 September 2011 |
| Rev.3: sponsor's change of address | 6 February 2015 |
| Disclaimer<br>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 17 April 2003, orphan designation (EU/3/03/140) was granted by the European Commission to Chiron Corporation Limited, United Kingdom, for tobramycin (inhalation powder) for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis.

The sponsorship was transferred to Novartis Europharm Limited, United Kingdom, in October 2006.

### What is Pseudomonas aeruginosa lung infection in cystic fibrosis?

Cystic fibrosis is a genetic disease. The genetic information that determines the characteristics of each individual is carried by genes located on structures called chromosomes. In humans, each cell has 23 pairs of chromosomes. For each pair one chromosome is inherited from the mother and the other from the father. Cystic fibrosis is caused by abnormalities of a specific gene, called CFTR, carried by the 7$^{th}$ pair of chromosomes. The CFTR gene is responsible for the production of a protein that regulates outflow of water and salts (like chloride) from cells that cover internal and external surfaces of the body, the so-called epithelial cells. Cystic fibrosis appears only when the CFTR is abnormal on both chromosomes of the 7$^{th}$ pair. The defective transport of water and salts due to the lack of the regulatory protein results in the thickening of the secretions in several organs (e.g. lungs, pancreas). This leads to chronic infection of the lungs and chronic inflammation (a response to the injury caused to the tissue). *Pseudomonas aeruginosa* is a species of bacteria (micro-organisms that can cause certain types of infections). Chronic infection of the lung with *Pseudomonas aeruginosa* is a typical

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feature of cystic fibrosis. It can induce damage to the lung tissue and respiratory insufficiency, which is life threatening.

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

At the time of designation, *Pseudomonas aeruginosa* lung infection in cystic fibrosis affected approximately 1.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 50,000 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?

*Pseudomonas aeruginosa* lung infection in cystic fibrosis is treated mostly with antibiotic (drugs that kill micro-organisms) therapy administered by a variety of routes, oral, intravenous and as an aerosol via nebulisation. Several antibiotics had been authorised for the condition in some countries in the Community, at the time of submission of the application for orphan designation. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that tobramycin (inhalation powder) might be of potential significant benefit for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis, particularly in regards to a contribution to patient care. The assumption of benefit is yet to be validated and 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?

Tobramycin is an antibiotic produced by certain strains of bacteria with activity against a wide range microorganisms including *Pseudomonas aeruginosa*. The sponsor has developed a formulation for dry powder inhalation to be administered with a commercial device. It acts by disrupting protein synthesis and this kills the microorganisms.

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

The evaluation of the effects of tobramycin (inhalation powder) in experimental models is ongoing.

At the time of the submission of the application for orphan designation clinical trials with tobramycin inhalation powder in cystic fibrosis patients with *Pseudomonas aeruginosa* lung infection had not been initiated.

Tobramycin inhalation powder was not marketed anywhere worldwide for the condition, at the time of submission and has not been submitted or approved for a marketing authorisation in any country.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 February 2003 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.
At the time of designation, this represented a population of 382,800,000 (Eurostat 2003).

Update: Tobramycin (inhalation powder) (Tobi Podhaler) has been authorised in the EU since 20 July 2011 for the suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in adults and children aged 6 years and older with cystic fibrosis.

More information on Tobi Podhaler can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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:

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom
Tel. +41 61 324 11 11 (Switzerland)
E-mail: orphan.enquiries@novartis.com

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 | Tobramycin (inhalation powder) | Treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis |
| Bulgarian | Тобрамицин (Прах за инхалация) | Лечение на *Pseudomonas aeruginosa* белодробна инфекция при кистична фиброза |
| Czech | Tobramycin ( inhalační forma-prášek) | Léčba plicních infekcí vyvolaných Pseudomonádou *aeruginosa* při cystické fibróze |
| Danish | Tobramycin (inhalationspulver) | Behandling af lungeinfektion med *Pseudomonas aeruginosa* ved cystisk fibrose |
| Dutch | Tobramycine (inhalatiepoeder) | Behandeling van *Pseudomonas aeruginosa* longinfectie bij cystische fibrosis |
| Estonian | Tobramütsiin (inhalatsiooni pulber) | *Pseudomonas aeruginosa* poolt põhjustatud kopsuinfektsiooni ravi tsüstilise fibroosi korral |
| Finnish | Tobramysiini (inhalaatiojauhe) | *Pseudomonas aeruginosan* aiheuttaman keuhkoinfektion hoito kystisessä fibroosissa |
| French | Tobramycine (poudre pour inhalation) | Traitement des infections pulmonaires à *Pseudomonas aeruginosa* dans la mucoviscidose |
| German | Tobramycin (Puder zur Inhalation) | Therapie der *Pseudomonas aeruginosa*-Infektion der Lunge bei zystischer Fibrose |
| Greek | Τομπραμυκίνη (κόνις για εισπνοή) | θεραπεία λοιμώξεων των πνευμόνων με *Pseudomonas aeruginosa* κατά την κυστική ίνωση |
| Hungarian | Tobramycin (por inhalációhoz) | *Pseudomonas aeruginosa* okozta tüdőfertőzés kezelése cisztikus fibrózisban |
| Italian | Tobramicina (polvere per inalazione) | Trattamento di infezione polmonare da *Pseudomonas aeruginosa* nella fibrosi cistica |
| Latvian | Tobramicīns (inhalācijas pulveris) | *Pseudomonas aeruginosa* izraisītas plaušu infekcijas ārstēšana cistiskās fibrozes gadījumā |
| Lithuanian | Tobramicinas (inhaliaciniai milteliai) | Plaučių infekcijos, sukeltos *Pseudomonas aeruginosa*, gydymas, sergant cistine fibroze |
| Maltese | Tobramycin (trab li jittieħed bin-nifs) | Kura ta' infezzjoni fil-pulmun mill-*Pseudomonas aeruginosa* fil-fibroži ċistiku |
| Polish | Tobramycyna (proszek do inhalacji) | Leczenie zapalenia płuc wywołanych przez *Pseudomonas aeruginosa* w przebiegu zwłóknienia torbielowatego |
| Portuguese | Tobramicina (pó para inalação) | Tratamento de infecção pulmonar por *Pseudomonas aeruginosa* na fibrosa quística |
| Romanian | Tobramicină (pulbere de inhalat) | Tratamentul infecţiei pulmonare cu *Pseudomonas aeruginosa* la pacienţii cu fibroză chistică |
| Slovak | Tobramycín (inhalačný prášok) | Liečba infekcií pľúc s *Pseudomonas aeruginosa* pri cystickej fibróze |

[1] At the time of marketing authorisation.

| Language | Active ingredient | Indication |
|---|---|---|
| Slovenian | Tobramicin (prašek za inhaliranje) | Zdravljenje pljučnice povzročene s *Pseudomonasom aeruginosa* pri cistični fibrozi |
| Spanish | Tobramicina (polvo para inhalacion) | Tratamiento de las infecciones pulmonares por *Pseudomonas aeruginosa* en la fibrosis quística |
| Swedish | Tobramycin (inhalationspulver) | Behandling av lunginflammation orsakad av *Pseudomonas aeruginosa* vid cystisk fibros |