22 June 2017
EMA/COMP/277117/2017

Public summary of opinion on orphan designation

Tamoxifen citrate for the treatment of cystic fibrosis

On 22 May 2017, orphan designation (EU/3/17/1877) was granted by the European Commission to GB Pharma Srl, Italy, for tamoxifen citrate for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects the secretion of fluids from cells in the lungs and from the glands in the gut and pancreas. In cystic fibrosis, these fluids become thick, blocking the airways in the lungs and the flow of digestive juices in the gut and pancreas. This leads to inflammation and long-term infection of the lungs because of the build-up of thick mucus, and to poor growth and nutrition because of problems with the digestion and absorption of food.

Cystic fibrosis is caused by changes (mutations) in a gene that makes a protein called 'cystic-fibrosis transmembrane conductance regulator' (CFTR), which is involved in regulating the production of mucus and digestive juices.

Cystic fibrosis is a long-term debilitating and life-threatening disease because it severely damages the lung tissue, leading to problems with breathing and to recurrent chest infections.

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

At the time of designation, cystic fibrosis affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 52,000 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?

At the time of designation, Kalydeco (ivacaftor) and Orkambi (ivacaftor and lumacaftor) were authorised to treat patients with cystic fibrosis who have certain mutations in the gene for CFTR. Lung infection in cystic fibrosis was mainly treated with antibiotics. Other medicines used to treat the lung disease included anti-inflammatory medicines, bronchodilators (medicines that help to open up the

[*]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 515,700,000 (Eurostat 2017).

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airways in the lungs) and mucolytics (medicines that help break down mucus in the lungs). In addition, patients with cystic fibrosis were often given other types of medicines such as pancreatic enzymes (substances that help to digest and absorb food) and food supplements. They were also advised to exercise and to have physiotherapy.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with cystic fibrosis. Laboratory studies showed that this medicine improved production of normal fluids in patients with certain mutations in the CFTR gene compared with Orkambi. Beneficial effects are not expected to be limited just to these mutations. 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?

Tamoxifen citrate is thought to increase the activity of a protein called calcium-dependent chloride channel (CaCC) which is also involved in regulating the production of mucus and digestive juices. This is expected to thin the abnormal secretions in cystic fibrosis, reducing symptoms of the disease and improving lung function.

What is the stage of development of this medicine?

The effects of tamoxifen citrate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with tamoxifen citrate in patients with cystic fibrosis were ongoing.

At the time of submission, tamoxifen citrate was authorised in the EU for the treatment of breast cancer.

At the time of submission, tamoxifen citrate was not authorised anywhere in the EU for the treatment of cystic fibrosis 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 11 April 2017 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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Tamoxifen citrate	Treatment of cystic fibrosis
Bulgarian	Тамоксифен цитрат	Лечение на кистозна фиброза
Croatian	Tamoksifen citrat	Liječenje cistične fibroze
Czech	Tamoxifencitrat	Léčba cystické fibrózy
Danish	Tamoxifen citrate	Behandling af cystisk fibrose
Dutch	Tamoxifen citrate	Behandeling van cystische fibrose
Estonian	Tamoksifeeni tsitraat	Tsüstilise fibroosi ravi
Finnish	Tamoksifeeni sitraatti	Kystisen fibroosin hoito
French	Tamoxifène citrate	Traitement de la mucoviscidose
German	Tamoxifencitrat	Behandlung zystischer Fibrose
Greek	Κιτρική ταμοξιφαίνη	Θεραπεία της κυστικής ίνωσης
Hungarian	Tamoxifen citrát	Cisztikus fibrózis kezelése
Italian	Tamoxifene citrato	Trattamento della fibrosi cistica
Latvian	Tamoksifēna citrāts	Cistiskās fibrozes ārstēšana
Lithuanian	Tamoksifenas citratas	Cistinės fibrozės gydymas
Maltese	Ċitrat tat-tamossifen	Kura tal-fibrożi ċistiku
Polish	Cytrynian tamoksyfenu	Leczenie zwłóknienia torbielowatego
Portuguese	Citrato de tamoxifeno	Tratamento da fibrose quística
Romanian	Tamoxifen citrat	Tratamentul fibrozei chistice
Slovak	Tamoxifen citrát	Terapia cystickej fibrózy
Slovenian	Tamoksifen citrat	Zdravljenje cistične fibroze
Spanish	Tamoksifeno citratas	Tratamiento de la fibrosis quística
Swedish	Tamoxifencitrat	Behandling av cystisk fibros
Norwegian	Tamoxifensitrat	Behandling av cystisk fibrose
Icelandic	Tamoxifen sítrat	Meðferð við slímseigjusjúkdómi

[1] At the time of designation