



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxy)methyl}-2,3-dihydroimidazo[2,1-b]oxazole for the treatment of tuberculosis

First publication	25 May 2008
Rev.1: administrative update	10 July 2008
Rev.2: transfer of sponsorship	15 November 2011
Rev.3: information about Marketing Authorisation	4 June 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 1 February 2008, orphan designation (EU/3/07/524) was granted by the European Commission to Otsuka Pharmaceutical Europe Ltd, United Kingdom, for (R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxy)methyl}-2,3-dihydroimidazo[2,1-b]oxazole for the treatment of tuberculosis.

The sponsorship was transferred to Otsuka Novel Products GmbH, Germany, in September 2011.

What is tuberculosis?

Tuberculosis is an infection caused by a group of bacteria called *Mycobacterium*. It spreads from person-to-person by inhaling the infected airborne droplets generated by sneezing and coughing. The manifestation of the disease is variable and not all patients who are infected will develop the disease. The disease is characterised by fever, cough and breathing difficulties. The infection by the tuberculosis bacteria induces formation of granulomas, which are accumulations of large numbers of cells leading to chronic inflammatory lesions. Granulomas can develop in any tissue, but occur most often in the lungs (pulmonary tuberculosis). Tuberculosis can also affect the central nervous system (meningitis), lymphatic system, genitourinary system, bones and joints. Tuberculosis is a life-threatening condition.



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

At the time of designation, tuberculosis affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of 101,000 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?

Treatment of tuberculosis consists of the administration of a combination of antibiotics for long periods of time.

Several medicinal products were authorised for the condition 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 (R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazole might be of potential significant benefit for the treatment of tuberculosis mainly because it might improve the long-term outcome of the patients. The assumption of benefit 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?

(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazole inhibits the production of mycolic acid, which is an exclusive component of the external wall of mycobacteria, the bacteria causing tuberculosis. The cell wall protects the bacteria from the outside and from external aggressions; its disruption can kill the bacteria.

What is the stage of development of this medicine?

The effects of (R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazole were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with tuberculosis were ongoing.

(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazole was not authorised anywhere worldwide for treatment of tuberculosis, at the time of submission. Orphan designation was granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 December 2007 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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 502,800,000 (Eurostat 2008).

Update: (R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxy-methyl}-2,3-dihydroimidazo[2,1-b]oxazole (Deltiba) has been authorised in the EU since 28 April 2014 for use as part of an appropriate combination regimen for pulmonary multi-drug resistant tuberculosis (MDR-TB) in adult patients when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.

More information on Deltiba 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](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports)

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:

Otsuka Novel Products GmbH
Erika-Mann-Strasse 21
80636 Muenchen
Germany

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](http://orphanet.eu), a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- [European Organisation for Rare Diseases \(EURORDIS\)](http://eurordis.eu), 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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazole	Treatment of tuberculosis
Bulgarian	(R)-2-Метил-6-нитро-2-{4-[4-(4-трифлуорометоксифенокси)пиперидин-1-ил]феноксиметил}-2,3-дихидроимидазо[2,1-b]оксазол	Лечение на туберкулоза
Czech	(R)-2-methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]fenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazol	Léčba tuberkulózy
Danish	(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazol	Behandling af tuberkulose
Dutch	(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluormethoxyphenoxy)piperidin-1-yl]fenoxyethyl}-2,3-dihydro-imidazo[2,1-b]oxazol	Behandeling van tuberculose
Estonian	(R)-2-metüül-6-nitro-2-{4-[4-(4-trifluoromeoksüfenoksü)piperidiin-1-üül]fenoksümetüül}-2,3-dihüdroimidaso[2,1-b]oksasool	Tuberkuloosi ravi
Finnish	(R)-2-metyyli-6-nitro-2-{4-[4-(4-trifluorometoksifenoksi)piperidiini-1-yyli]fenoksimetyyli}-2,3-dihydroimidatso[2,1-b]oksatsoli	Tuberkuloosin hoito
French	(R)-2-méthyl-6-nitro-2-{4-[4-(4-trifluorométhoxyphénoxy)pipéridine-1-yl]phénoxyéthyl}-2,3-dihydroimidazo[2,1-b]oxazole	Traitement de la tuberculose
German	(R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluormethoxyphenoxy)piperidin-1-yl]phenoxyethyl}-2,3-dihydroimidazo[2,1-b]oxazol	Behandlung der Tuberkulose
Greek	(R)-2-Μεθυλ-6-νιτρο-2-{4-[4-(4-τριφθορομεθοξυφαινοξυ)πιπεριδίνη-1-υλ]φαινοξυμεθυλ}-2,3-διυδροϊμιδαζο[2,1-b]οξαζόλη	Θεραπεία της φυματίωσης

¹ At the time of designation

Language	Active Ingredient	Indication
Hungarian	(R)-2-metil-6-nitro-2-{ 4-[4-(4-trifluorometoxifenoxi)piperidin-1-il]fenoximetil}-2,3-dihidroimidazo[2,1-b]oxazol	Tuberculosis kezelése
Italian	(R)-2-Metil-6-nitro-2-{ 4-[4-(4-trifluorometossifenossi)piperidin-1-il]fenossimetil}-2,3-diidroimidazo[2,1-b]ossazolo	Trattamento della tubercolosi
Latvian	(R)-2-Metil-6-nitro-2-{ 4-[4-(4-trifluorometoksifenoksi)piperidīn-1-il]fenoksimetil}-2,3-dihidroimidazo[2,1-b]oksazols	Tuberkulozes ārstēšana
Lithuanian	(R)-2-metil-6-nitro-2-{ 4-[4-(4-trifluorometoksifenoksi)piperidin-1-il]fenoksimetil}-2,3-dihidroimidazo[2,1-b]oksazolas	Tuberkuliozės gydymas
Maltese	(R)-2-Methyl-6-nitro-2-{ 4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxymethyl}-2,3-dihydroimidazo[2,1-b]oxazole	Kura tat-tuberkulosi
Polish	(R)-2-Metylo-6-nitro-2-{ 4-[4-(4-trifluorometoksyfenoksy)piperydyn-1-yl]fenoksymetyl}-2,3-dihydroimidazo[2,1-b]oksazol	Leczenie gruźlicy
Portuguese	(R)-2-Metil-6-nitro-2-{ 4-[4-(4-trifluorometoxifenoxi)piperidin-1-il]fenoximetil}-2,3-dihidroimidazo[2,1-b]oxazol	Tratamento da tuberculose
Romanian	(R)-2-Metil-6-nitro-2-{ 4-[4-(4-trifluorometoxifenoxi)piperidin-1-il]fenoximetil}-2,3-dihidroimidazo[2,1-b]oxazol	Tratamentul tuberculozei
Slovak	(R)-2-metyl-6-nitro-2-{ 4-[4-(4-trifluórmetyoxyfenoxy)piperidín-1-yl]fenoxymetyl}-2,3-dihydroimidazo[2,1-b]oxazol	Liečba tuberkulózy
Slovenian	(R)-2-metil-6-nitro-2-{ 4-[4-(4-trifluorometoksifenoksi)piperidin-1-il]fenoksimetil}-2,3-dihidroimidazo[2,1-b]oksazol	Zdravljenje tuberkuloze
Spanish	(R)-2-metil-6-nitro-2-{ 4-[4-(4-trifluorometoxifenoxi)piperidín-1-il]fenoximetil}-2,3-dihidroimidazo[2,1-b]oxazol	Tratamiento de la tuberculosis

Language	Active Ingredient	Indication
Swedish	(R)-2-metyl-6-nitro-2-{4-[4-(4-trifluorometoxifenoxi)piperidin-1-yl]fenoximetyl}-2,3-dihydroimidazo[2,1-b]oxazol	Behandling av tuberkulos
Norwegian	(R)-2-metyl-6-nitro-2-{4-[4-(4-trifluormetoksyfenoksy)piperidin-1-yl]fenoksymetyl}-2,3-dihydroimidazo[2,1-b]oksazol	Behandling av tuberkulose
Icelandic	(R)-2-metýl-6-nítro-2-{4-[4-(4-tríflúorómetoxýfenoxý)píperidín-1-yl]fenoxýmetýl}-2,3-dihýdróímidazó[2,1-b]oxazól	Meðferð við berklum