17 March 2014
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol for the treatment of tuberculosis

First publication	4 January 2006
Rev.1: transfer of sponsorship	12 August 2009
Rev.2: transfer of sponsorship	18 June 2012
Rev.3: administrative update	11 February 2013
Rev.4: information about Marketing Authorisation	17 March 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 26 August 2005, orphan designation (EU/3/05/314) was granted by the European Commission to Tibotec Pharmaceuticals Ltd., Ireland, for (1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol for the treatment of tuberculosis.

The sponsorship was transferred to Tibotec BVBA, Belgium, in December 2008 and to Janssen-Cilag International N.V., Belgium, in September 2012.

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. Granulomas (accumulation of a large number of cells leading to chronic inflammatory lesions) can develop in any body tissue, but most often in the lungs (pulmonary TB) but can also affect the central nervous system (meningitis), lymphatic system, genitourinary system, bones and joints. Tuberculosis is a life-threatening condition.

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

At the time of designation, tuberculosis affected not more than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 92,000 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 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.

The sponsor has provided sufficient information to show that (1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol might be of significant benefit for patients with tuberculosis because it might improve the long-term outcome of the patients.

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?

(1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol is according to the sponsor an anti-mycobacterial agent. It acts by blocking (inhibiting) a protein involved in the energy generation of the mycobacteria and this could potentially kill the microorganism itself.

What is the stage of development of this medicine?

The effects of (1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol were evaluated in experimental models.

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

(1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol was not authorised anywhere worldwide for treatment of tuberculosis 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 13 July 2005 recommending the granting of this designation.

Update: (1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol (Sirturo) has been authorised in the EU since 05 March 2014. Sirturo is ndicated for use as part of an appropriate combination regimen for pulmonary multidrug resistant tuberculosis (MDR TB) in adult patients when an effective treatment regimen cannot otherwise be

* 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 466,600,000 (Eurostat 2005).

composed for reasons of resistance or tolerability. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

More information on Sirturo 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:

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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	(1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol	Treatment of tuberculosis
Bulgarian	(1R,2S) 6-бромо-алфа-[2-(диметиламино) етил]-2-метокси-алфа-(1-нафтил)-бета-фенил-3-кинолинетанол	Лечение на туберкулоза
Czech	(1R,2S) 6-bromo-alfa-[2-(dimetylamino)etyl]-2-metoxy-alfa-(1-naftylo)-beta-fenyl-3-chinolino-etanol	Léčba tuberkulózy
Danish	(1R,2S) 6-bromo-alpha-[2-(dimetylamino)etyl]-2-metoxy-alpha-(1-naphtyl)-beta-fenyl-3-quinolineetanol	Behandling af tuberkulose
Dutch	(1R,2S) 6-broom-alfa-[2-(dimethylamino)ethyl]-2-methoxy-alfa-(1-naftyl)-bèta-fenyl-3-chinoline-ethanol	Behandeling van tuberculose
Estonian	(1R,2S) 6-bromo-alfa-[2-(dimetüülamino)etüül]-2-metoksü-alfa-(1-naftüül)-beeta-fenüül-3-kinoliinetanool	Tuberkuloosi ravi
Finnish	(1R,2S) 6-bromo-alfa-[2-(dimetyyliamino)etyyli]-2-metoksi-alpha-(1-naftyyli)-beta-fenyyli-3-quinoliinietanoli	Tuberkuloosin hoito
French	(1R,2S) 6-bromo-alpha-[2-(diméthylamino)éthyl]-2-méthoxy-alpha-(1-naphthyl)-bêta-phényl-3-quinolineéthanol	Traitement de la tuberculose
German	(1R,2S) 6-Bromo-Alpha-[2-(Dimethylamino)Ethyl]-2-Methoxy-Alpha-(1-Naphthyl)-Beta-Phenyl-3-Chinolinethanol	Behandlung der Tuberkulose
Greek	(IR, 2S) 6- βρώμο- άλφα [2-(διμεθυλάμινο) αίθυλ}-2- μεθόξυ-αλφά-(1-ναφθυλ)-βήτα-φαινύλ-3-κινολιναιθανόλη	Θεραπεία της φυματίωσης
Hungarian	(1R,2S) 6-brom-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3- quinolinethanol	Tuberculosis kezelése
Italian	(1R,2S) 6-bromo-alfa-[2-(dimetilamino)etil]-2-metossi-alfa-(1-naftil)-beta-fenil-3-chinolinaetanolo	Trattamento della tubercolosi
Latvian	(1R,2S) 6-bromo-alfa-[2-(dimetilamīn)etil]-2-metoksi-alfa-(1-naftil)-beta-fenil-3-kvinolīnetanols	Tuberkulozes ārstēšana

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Lithuanian	(1R,2S) 6-bromo-alfa-[2-(dimetilamino)etil]-2-metoksi-alfa-(1-naftil)-beta-fenil-3- kvinolinetanolis	Tuberkuliozės gydymas
Maltese	(1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethanol	Kura tat-tuberkulosi
Polish	(1R,2S) 6-bromo-alfa-[2-(dimetyloamino)etyl]-2-metoksy-alfa-(1-naftylo)-beta-fenyl-3-chinolino-etanol	Leczenie gruźlicy
Portuguese	(1R,2S) 6-bromo-alfa-[2-(dimetilamino)etil]-2-metoxy-alfa-(1-naftil)-beta-fenil-3-quinolineetanol	Tratamento da tuberculose
Romanian	(1R, 2S) 6-bromo-alfa-[2(dimetilamino)etil]-2-metoxi-alfa-(1-naftil)-beta-fenil-3-quinolinoetanol	Tratamentul tuberculozei
Slovak	(1R,2S) 6-bromo-alfa-[2-(dimetylamino)etyl]-2-metoxy-alfa-(1-naftyl)-beta-fenyl-3-chinolínetanol	Liečba tuberkulózy
Slovenian	(1R, 2S) 6-bromo-alfa-[2-(dimetilamino)etil]-2-metoksi-alfa-(1-naftil)-beta-fenil-3- kinolinetanol	Zdravljenje tuberkoloze
Spanish	(1R, 2S) 6-bromo-alfa-[2-(dimetilamino)etil]-2-metoxi-alfa-(1-naftil)-beta-fenil-3-quinolinetanol	Tratamiento de la tuberculosis
Swedish	(1R,2S) 6-bromo-alfa-[2-(dimetylamino)etyl]-2-metoxi-alfa-(1-naftyl)-beta-fenyl-3-kinolinetanol	Behandling av tuberkulos
Norwegian	(1R,2S) 6-bromo-alfa-[2-(dimetylamino)etyl]-2- metoksy -alfa-(1-naftyl)-beta-fenyl-3-kinolinetanol	Behandling av tuberkulose
Icelandic	(1R, 2S) 6-brómó-alfa-[2-(tvímetýlamínó)etýl]-2-metoxý-alfa-(1-naftýl)-beta-fenýl-3-kínólínetanól	Meðferð við berklum