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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Para-aminosalicylic acid for the treatment of tuberculosis

First publication	18 January 2011
Rev.1: transfer of sponsorship	19 March 2012
Rev.2: sponsor's change of address	13 September 2013
Rev.3: information about Marketing Authorisation	4 June 2014
Rev.4: administrative update	14 October 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 17 December 2010, orphan designation (EU/3/10/826) was granted by the European Commission to Lucane Pharma SAS, France, for para-aminosalicylic acid for the treatment of tuberculosis.

The sponsorship was transferred to Lucane Pharma SA, France, in February 2012.

What is tuberculosis?

Tuberculosis (TB) is an infectious disease caused by bacteria called *Mycobacterium tuberculosis*. People become infected by inhaling infected droplets from the cough or sneeze of people who have the disease. TB primarily affects the lungs (when it is called pulmonary TB) but it can also spread to other parts of the body, such as the bones or the nervous system. The symptoms of TB include persistent cough, fever, weight loss and night sweats. Not everyone infected will develop the symptoms of the disease.

TB is a long-term debilitating disease. When left untreated, the disease may be life threatening, mainly because of the severe damage to the lungs that does not allow the patient to breathe normally, and because the bacteria causing the disease are often resistant to existing treatments.

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

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

At the time of designation, several antibiotics were authorised in the EU to treat TB. These were used in combination and for long periods of time, normally at least six months.

The sponsor has provided sufficient information to show that para-aminosalicylic acid might be of significant benefit for patients with TB because it is expected to improve the treatment of patients with TB that is resistant to many other medicines, and because it will be available as a gastroresistant granule formulation that is expected to cause fewer side effects. These assumptions 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?

Medicines containing para-aminosalicylic acid have been used in combination with other medicines to treat TB since the 1940s. Para-aminosalicylic acid is a 'bacteriostatic'. This means that it prevents the bacteria from growing and multiplying without actually killing them. It does this by blocking the synthesis (manufacture) of folic acid, which the bacteria need to grow and multiply, and of mycobactin, a component of their cell wall. These actions have the effect of stopping the growth of bacteria also in patient with TB that is resistant to other antibiotics like streptomycin and isoniazid.

In this medicine, para-aminosalicylic acid is expected to be available as gastroresistant granules that allow the para-aminosalicylic acid to reach the intestine without being released in the stomach, thus avoiding irritation in the stomach and causing fewer side effects.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with para-aminosalicylic acid in patients with TB had finished.

At the time of submission, para-aminosalicylic acid was authorised in the United States of America and Russia for TB.

At the time of submission, the medicine was not authorised anywhere in the EU for TB. Orphan designation of para-aminosalicylic acid for TB had been granted in the United States of America.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 October 2010 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 506,300,000 (Eurostat 2010).

Update: para-aminosalicylic acid (Granupas, previously Para-aminosalicylic acid Lucane) has been authorised in the EU since 7 April 2014 for use as part of an appropriate combination regimen for multi-drug resistant tuberculosis in adults and paediatric patients from 28 days of age and older when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.

More information on Granupas 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	Para-aminosalicylic acid	Treatment of tuberculosis
Bulgarian	Пара-аминосалицилова киселина	Лечение на туберкулоза
Czech	Para-aminosalicylic kyselina	Léčba tuberkulózy
Danish	Para-aminosalicylsyre	Behandling af tuberkulose
Dutch	Para-aminosalicylzuur	Behandeling van tuberculose
Estonian	Para-aminosalitsüülehape	Tuberkuloosi ravi
Finnish	Para-aminosalisyylihappo	Tuberkuloosin hoito
French	Acide para-aminosalicylique	Traitement de la tuberculose
German	Paraaminosalicylsäure	Behandlung der Tuberkulose
Greek	Παρα-αμινοσαλικυλικό οξύ	Θεραπεία της φυματίωσης
Hungarian	Para-aminoszalicilsav	Tuberculosis kezelése
Italian	Acido para-aminosalicilico	Trattamento della tubercolosi
Latvian	Para-aminosalicilskābe	Tuberkulozes ārstēšana
Lithuanian	Para-aminosalicilo rūgštis	Tuberkuliozės gydymas
Maltese	Para-aminosalicylic acid	Kura tat-tuberkulosi
Polish	Kwas paraaminosalicylowy	Leczenie gruźlicy
Portuguese	Ácido para-aminossalicílico	Tratamento da tuberculose
Romanian	Acid para-aminosalicilic	Tratamentul tuberculozei
Slovak	Kyselina paraaminosalicylová	Liečba tuberkulózy
Slovenian	Para-aminosalicilna kislina	Zdravljenje tuberkoloze
Spanish	Ácido paraaminosalicílico	Tratamiento de la tuberculosis
Swedish	Para-aminosalicylsyra	Behandling av tuberkulos
Norwegian	Para-aminosalisylsyre	Behandling av tuberkulose
Icelandic	Para-amínósalicýlic sýru	Meðferð við berklum

[1] At the time of designation