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EMA/COMP/391429/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Melatonin for the treatment of neonatal sepsis

On 27 June 2016, orphan designation (EU/3/16/1683) was granted by the European Commission to Therapicon Srl, Italy, for melatonin for the treatment of neonatal sepsis.

What is neonatal sepsis?

Neonatal sepsis is a severe bacterial infection of the blood in newborn babies. The infection is mostly caused by bacteria, but other types of organisms (e.g. viruses and fungi) may also be involved. The baby may become infected during birth with microorganisms in the mother's body. The infection may also result from medical procedures such as use of a machine to help with breathing and giving medicines and feeds through a vein.

Premature babies born at least 8 weeks early are at a higher risk of sepsis than babies born at term. This is because their immune system (the body's natural defences), skin and moist body surfaces are not yet fully developed.

Sepsis is a life-threatening condition which may cause multiple organ failure.

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

At the time of designation, neonatal sepsis affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000 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, antibiotic, antiviral and antifungal medicines were commonly used to treat neonatal sepsis.

The sponsor has provided sufficient information to show that melatonin might be of significant benefit for patients with neonatal sepsis because published studies have shown improvement in the condition

^{*}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 513,700,000 (Eurostat 2016).

when melatonin was added to conventional treatment. 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?

Melatonin is a natural substance produced in the body with a variety of activities. It is involved in controlling sleep patterns, it also stimulates the production of many enzymes and acts as an antioxidant (a substance that helps the body protect itself against damage due to reactive substances containing oxygen). The exact way in which melatonin could work in neonatal sepsis is not clearly understood. It is thought that antibacterial and antiviral activities of melatonin given by injection may be linked to activation of certain protective enzymes.

What is the stage of development of this medicine?

The effects of melatonin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with melatonin in patients with neonatal sepsis had been started.

At the time of submission, melatonin given by mouth as tablets was authorised in the EU for short-term treatment of insomnia.

At the time of submission, melatonin was not authorised anywhere in the EU for neonatal sepsis 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 19 May 2016 recommending the granting of this designation.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Melatonin	Treatment of neonatal sepsis
Bulgarian	Мелатонин	Лечение на неонатален сепсис
Croatian	Melatonin	Liječenje novorođenačke sepsе
Czech	Melatonin	Léčba sepsе novorozenců
Danish	Melatonin	Behandling af neonatal sepsis
Dutch	Melatonine	Behandeling van neonatale sepsis
Estonian	Melatoniin	Vastsündinute sepsise ravi
Finnish	Melatoniiini	Vastasyntyneen sepsiksen hoito
French	Mélatonine	Traitement de la septicémie néonatale
German	Melatonin	Behandlung der Neugeborenenensepsis
Greek	Μελαντονίνη	θεραπεία της νεογνικής σηψαιμίας
Hungarian	Melatonin	Újszülöttkori szepszis kezelése
Italian	Melatonina	Trattamento della sepsi neonatale
Latvian	Melatonīns	Jaundzimušo sepses ārstēšana
Lithuanian	Melatoninas	Naujagimių sepsio gydymas
Maltese	Melatonina	Trattament ta' sepsis fi trabi tat-twelid
Polish	Melatonina	Leczenie posocznicy noworodka
Portuguese	Melatonina	Tratamento da sépsis neonatal
Romanian	Melatonină	Tratamentul sepsis neonatal
Slovak	Melatonín	Liečba sepsy novorodencov
Slovenian	Melatonin	Zdravljenje neonatalne sepsе
Spanish	Melatonina	Tratamiento de la sepsis neonatal
Swedish	Melatonin	Behandling av neonatal sepsis
Norwegian	Melatonin	Behandling av neonatal sepsis
Icelandic	Melatónín	Meðferð við nýbura sýklasótt

¹ At the time of designation