

1 August 2016
EMA/COMP/391425/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Melatonin for the treatment of necrotising enterocolitis

On 1 August 2016, orphan designation (EU/3/16/1682) was granted by the European Commission to Therapicon Srl, Italy, for melatonin for the treatment of necrotising enterocolitis.

What is necrotising enterocolitis?

Necrotising enterocolitis is an inflammatory disease of the gut that affects preterm infants. In these infants, portions of the gut become inflamed and start to die. Symptoms may include problems with feeding, abdominal distension (bloating) and bloody stools. If the disease progresses, it can lead to tearing of the gut and the leakage of the contents of the gut into the abdomen causing peritonitis (infection of the abdominal cavity) and sepsis (infection of the blood).

Although the exact cause of necrotising enterocolitis is unclear, it is known that the gut and the immune system (the body's natural defence system) of preterm infants are immature and not as well developed as that of full term infants. In particular the intestinal flora, which consists of non-pathogenic (not causing disease) microorganisms that prevent the colonisation of pathogenic microorganisms in the gut, is altered, increasing the risk of injury and infection of the gut.

Necrotising enterocolitis is a severe and life-threatening disease that delays normal growth, causes malnutrition and can lead to complications such as gut perforation, sepsis and peritonitis.

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

At the time of designation, necrotising enterocolitis affected less than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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).

*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).

What treatments are available?

At the time of designation, there were no satisfactory methods authorised in the EU for the treatment of necrotising enterocolitis.

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 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 necrotising enterocolitis is not clearly understood but it is thought that its ability to increase production of the enzyme heme oxygenase-1 may be important, since lack of this enzyme has been linked to necrotising enterocolitis. It is expected that, by increasing the amount of this enzyme, injections of melatonin may help reduce the symptoms of necrotising enterocolitis.

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 the medicine in patients with necrotising enterocolitis 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, the medicine was not authorised anywhere in the EU for necrotising enterocolitis 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 necrotising enterocolitis
Bulgarian	Мелатонин	Лечение на некротизиращ ентероколит
Croatian	Melatonin	Liječenje nekrotizirajućeg enterokolitisa
Czech	Melatonin	Léčba nekrotizující enterokolitidy
Danish	Melatonin	Behandling af nekrotiserende enterokolitis
Dutch	Melatonine	Behandeling van necrotiserende enterocolitis
Estonian	Melatoniin	Nekrotiseeriva enterokoliidi ravi
Finnish	Melatoniiini	Nekrotisoivan suolitulehduksen hoito
French	Mélatonine	Traitement de l'entéocolite nécrosante
German	Melatonin	Behandlung von nekrotisierender Enterokolitis
Greek	Μελατονίνη	Θεραπεία νεκρωτικής εντεροκολίτιδας
Hungarian	Melatonin	Nekrotizáló enterocolitis kezelése
Italian	Melatonina	Trattamento dell'enterocolite necrotizzante
Latvian	Melatonīns	Nekrotizējošā enterokolīta ārstēšana
Lithuanian	Melatoninas	Nekrozuojančio enterokolito gydymas
Maltese	Melatonina	Kura tal-enterokolite bin-nekroži
Polish	Melatonina	Leczenie martwiczego zapalenia jelit
Portuguese	Melatonina	Tratamento de enterocolite necrosante
Romanian	Melatonină	Tratamentul enterocolitei necrozante
Slovak	Melatonín	Liečba nekrotizujúcej enterokolitídy
Slovenian	Melatonin	Zdravljenje nekrotizirajočega enterokolitisa
Spanish	Melatonina	Tratamiento de la enterocolitis necrotizante
Swedish	Melatonin	Behandling av nekrotisk enterokolit
Norwegian	Melatonin	Behandling av nekrotiserende enterokolitt
Icelandic	Melatónín	Meðferð garna - og ristilbólguðrepi

¹ At the time of designation