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EMA/COMP/48621/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lactobacillus reuteri for the prevention of necrotising enterocolitis

On 12 February 2015, orphan designation (EU/3/15/1436) was granted by the European Commission to Infant Bacterial Therapeutics AB, Sweden, for *Lactobacillus reuteri* for the prevention of necrotising enterocolitis.

What is necrotising enterocolitis?

Necrotising enterocolitis is an inflammatory disease of the gut that affects preterm infants. In infants with necrotising enterocolitis, 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 a perforation of the gut and the leakage of the contents of the gut into the abdomen causing peritonitis and sepsis (infection of the abdominal cavity and 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 at risk of developing the condition?

At the time of designation, the number of patients at risk of necrotising enterocolitis was estimated to be approximately 4.5 people in 10,000 per year in the European Union (EU). This was equivalent to a total of around 231,000 people per year*, 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 512,900,000 (Eurostat 2015).

What methods of prevention are available?

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

How is this medicine expected to work?

Lactobacillus reuteri is a bacterium that is normally found in the human gut. The way *L. reuteri* works in preventing necrotising enterocolitis is not fully elucidated, but there are 3 plausible mechanisms behind its effect: it may prevent pathogenic microorganisms from colonising the gut; it may have an anti-inflammatory effect; or it may improve gut mobility.

In preterm infants, giving these bacteria by mouth is expected to support the development of the normal intestinal flora, thereby preventing the development of necrotising enterocolitis.

What is the stage of development of this medicine?

The effects of the medicine 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 at risk of necrotising enterocolitis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for necrotising enterocolitis. Orphan designation of the medicine had been granted in the United States for necrotising enterocolitis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 January 2015 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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	<i>Lactobacillus reuteri</i>	Prevention of necrotising enterocolitis
Bulgarian	<i>Lactobacillus reuteri</i>	Превенция на некротизиращ ентероколит
Croatian	<i>Lactobacillus reuteri</i>	Prevenција nekrotizirajućeg enterokolitisa
Czech	<i>Lactobacillus reuteri</i>	Prevence nekrotizující enterokolitidy
Danish	<i>Lactobacillus reuteri</i>	Forebyggelse af nekrotiserende enterocolitis
Dutch	<i>Lactobacillus reuteri</i>	Preventie van necrotiserende enterocolitis
Estonian	<i>Lactobacillus reuteri</i>	Nekrotiseeriva enterokoliidi ennetamine
Finnish	<i>Lactobacillus reuteri</i>	Nekrotisoivan suolitulehduksen ehkäisy
French	<i>Lactobacillus reuteri</i>	Prévention de l'entérococolite nécrosante
German	<i>Lactobacillus reuteri</i>	Verhinderung von nekrotisierender Enterokolitis
Greek	<i>Lactobacillus reuteri</i>	Πρόληψη νεκρωτικής εντεροκολίτιδας
Hungarian	<i>Lactobacillus reuteri</i>	Nekrotizáló enterocolitis megelőzése
Italian	<i>Lactobacillus reuteri</i>	Prevenzione dell'enterocolite
Latvian	<i>Lactobacillus reuteri</i>	Nekrotizējošā enterokolīta profilakse
Lithuanian	<i>Lactobacillus reuteri</i>	Nekrozuojančio enterokolito prevencija
Maltese	<i>Lactobacillus reuteri</i>	Prevenzjoni tal-enterokolite bin-nekroži
Polish	<i>Lactobacillus reuteri</i>	Zapobieganie martwiczemu zapaleniu jelit
Portuguese	<i>Lactobacillus reuteri</i>	Prevenção de enterocolite necrosante
Romanian	<i>Lactobacillus reuteri</i>	Prevenția enterocolitei necrozante
Slovak	<i>Lactobacillus reuteri</i>	Prevenca nekrotizujúcej enterokolitídy
Slovenian	<i>Lactobacillus reuteri</i>	Preprečevanje nekrotizirajočega enterokolitisa
Spanish	<i>Lactobacillus reuteri</i>	Prevención de la enterocolitis necrotizante
Swedish	<i>Lactobacillus reuteri</i>	Förebyggande av nekrotisk enterokolit
Norwegian	<i>Lactobacillus reuteri</i>	Forebygging av nekrotiserende enterokolitt
Icelandic	<i>Lactobacillus reuteri</i>	Vörn gegn garna - og ristilbólguðrepi

¹ At the time of designation