



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

*Lactobacillus acidophilus* and *Bifidobacterium bifidum* for the prevention of necrotising enterocolitis

On 16 January 2014, orphan designation (EU/3/13/1213) was granted by the European Commission to Laboratorio Farmaceutico S.I.T. s.r.l., Italy, for *Lactobacillus acidophilus* and *Bifidobacterium bifidum* 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 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 life-threatening because it 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 less than 4.5 people in 10,000 per year in the European Union (EU). This was equivalent to a total of fewer than 230,000 people per year\*, and is below the ceiling for orphan designation, which is 5

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\*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 512,200,000 (Eurostat 2013).



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 methods of prevention are available?**

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

### **How is this medicine expected to work?**

*Lactobacillus acidophilus* and *Bifidobacterium bifidum* are so-called probiotics: bacteria that do not cause disease and that are normally found in the gut flora where they prevent pathogenic microorganisms from colonising the gut. Probiotics are currently used to prevent changes in the gut flora, due to modern diet and lifestyle as well as the use of antibiotics.

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

### **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 the medicine in patients with necrotising enterocolitis were ongoing.

At the time of submission, the medicine was authorised in some EU Member States to prevent changes in the gut flora.

At the time of submission, the medicinal product 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 6 November 2013 recommending the granting of this designation.

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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:

Laboratorio Farmaceutico S.I.T. s.r.l.  
Via Cavour 70,  
I-27035 Mede (PV)  
Italy  
Tel. +39 038 480 71  
Fax +39 080 737 0  
E-mail: [l.pedrotti@sit-farmaceutici.com](mailto:l.pedrotti@sit-farmaceutici.com)

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	<i>Lactobacillus acidophilus</i> and <i>Bifidobacterium bifidum</i>	Prevention of necrotising enterocolitis
Bulgarian	<i>Lactobacillus acidophilus</i> и <i>Bifidobacterium bifidum</i>	Превенция на некротизиращ ентероколит
Czech	<i>Bifidobacterium bifidum</i> a <i>Lactobacillus acidophilus</i>	Prevence nekrotizující enterokolitidy
Croatian	<i>Bifidobacterium bifidum</i> and <i>Lactobacillus acidophilus</i>	Prevenција nekrotizirajućeg enterokolitisa
Danish	<i>Bifidobacterium bifidum</i> og <i>Lactobacillus acidophilus</i>	Forebyggelse af nekrotiserende enterocolitis
Dutch	<i>Lactobacillus acidophilus</i> en <i>Bifidobacterium bifidum</i>	Preventie van necrotiserende enterocolitis
Estonian	<i>Lactobacillus acidophilus</i> ja <i>Bifidobacterium bifidum</i>	Nekrotiseeriva enterokoliidi ennetamine
Finnish	<i>Bifidobacterium bifidum</i> ja <i>Lactobacillus acidophilus</i>	Nekrotisoivan suolitulehduksen ehkäisy
French	<i>Bifidobacterium bifidum</i> et <i>Lactobacillus acidophilus</i>	Prévention de l'entérocolite nécrosante
German	<i>Bifidobacterium bifidum</i> und <i>Lactobacillus acidophilus</i>	Verhinderung von nekrotisierender Enterokolitis
Greek	<i>Bifidobacterium bifidum</i> και <i>Lactobacillus acidophilus</i>	Πρόληψη νεκρωτικής εντεροκολίτιδας
Hungarian	<i>Bifidobacterium bifidum</i> és <i>Lactobacillus acidophilus</i>	Nekrotizáló enterocolitis megelőzése
Italian	<i>Bifidobacterium bifidum</i> e <i>Lactobacillus acidophilus</i>	Prevenzione dell'enterocolite
Latvian	<i>Bifidobacterium bifidum</i> un <i>Lactobacillus acidophilus</i>	Nekrotizējošā enterokolīta profilakse
Lithuanian	<i>Lactobacillus acidophilus</i> ir <i>Bifidobacterium bifidum</i>	Nekrozuojančio enterokolito prevencija
Maltese	<i>Bifidobacterium bifidum</i> u <i>Lactobacillus acidophilus</i>	Prevenzjoni tal-enterokolite bin-nekroži
Polish	<i>Bifidobacterium bifidum</i> i <i>Lactobacillus acidophilus</i>	Zapobieganie martwiczemu zapaleniu jelit

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Portuguese	<i>Bifidobacterium bifidum</i> e <i>Lactobacillus acidophilus</i>	Prevenção de enterocolite necrosante
Romanian	<i>Bifidobacterium bifidum</i> și <i>Lactobacillus acidophilus</i>	Prevenția enterocolitei necrozante
Slovak	<i>Bifidobacterium bifidum</i> a <i>Lactobacillus acidophilus</i>	Prevenia nekrotizujúcej enterokolitídy
Slovenian	<i>Bifidobacterium bifidum</i> in <i>Lactobacillus acidophilus</i>	Preprečevanje nekrotizirajočega enterokolitisa
Spanish	<i>Bifidobacterium bifidum</i> y <i>Lactobacillus acidophilus</i>	Prevenición de la enterocolitis necrotizante
Swedish	<i>Bifidobacterium bifidum</i> och <i>Lactobacillus acidophilus</i>	Förebyggande av nekrotisk enterokolit
Norwegian	<i>Bifidobacterium bifidum</i> og <i>Lactobacillus acidophilus</i>	Forebygging av nekrotiserende enterokolitt
Icelandic	<i>Bifidobacterium bifidum</i> og <i>Lactobacillus acidophilus</i>	Vörn gegn garna - og ristilbólguðrepi