Opella Healthcare Italy
PACKAGING TEAM

For Opella use only

Code:	**940444**
Update:	V01 - 04-07-2025
GMID code:	925194
Current item code:	*925833*
Product/Item type:	*Istruzione Enterogermina 2 MLD - 10 flac.*
Country:	India
Artwork by:	Origgio
Plant:	Origgio

Technical Data

Format:	185 x 210 mm.
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Number of colours:	2
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Fonts:	Futura Book / Book Oblique / Bold / Bold Oblique
Minimum point size of text:	7 pt
Layout of Cutting:	N.A.
Packaging Line:	EG 096

GDO - *Graphic Department Origgio*
Opella Healthcare Italy S.r.l. - Viale Europa, 11
21040 Origgio (VA) - Italy - Tel. +39 - 02 96 10 559

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15 mm

Spores of polyantibiotic-resistant *Bacillus clausii*

Enterogermina® 2 billion/5mL oral suspension

sanofi

COMPOSITION
One 5mL mini bottle contains spores of polyantibiotic-resistant *Bacillus clausii* - 2 billion
(strains: O/C, N/R, SIN and T)

PHARMACEUTICAL FORM
Oral suspension

CLINICAL PARTICULARS
Therapeutic indications
For the treatment of alterations in the intestinal bacterial flora.

Posology and method of administration
Adults: 2-3 mini bottles per day
Children: 1-2 mini bottles per day
Infants: 1-2 mini bottles per day
unless prescribed otherwise by the doctor.

Administration at regular intervals, Take the mini bottle as it is or dilute it in water or other beverages (e.g., milk, tea, orange juice).

This medicinal product is for oral use only. Do not inject or administer through other routes (see Section Special warnings and special precautions for use).

Contraindications
Hypersensitivity to the active substance or to any of the excipients.

Special warnings and special precautions for use
Special warnings
Severe anaphylactic reactions, such as anaphylactic shock, have occurred with incorrect route of administration.
Any presence of visible corpuscles in the mini bottles of Enterogermina® is due to aggregates of *Bacillus clausii* spores; it does not therefore – suggest that the product has been altered.
Shake the mini bottle before use.
There have been reports of bacteremia, septicemia or sepsis in patients taking *Bacillus clausii* who are immunocompromised or are hospitalized due to a serious illness. Enterogermina® should be used in these patients only if the potential benefits outweigh the potential risks.
During treatment with antibiotics, it is recommended that the preparation be administered between antibiotic doses.

Interactions with other medicinal products and other forms of interaction.
No interaction studies have been performed.

Reproduction
Pregnancy
Limited data are available on the use of probiotics including Enterogermina® in pregnant women. However, no conclusions can be drawn regarding whether or not Enterogermina® is safe for use during pregnancy. Enterogermina® should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the fetus.

Lactation
There are limited available data on the presence of Enterogermina® in human milk, milk production, or the effects on the breastfed infant. However, no conclusions can be drawn regarding whether or not Enterogermina® is safe for use during breastfeeding. Enterogermina® should be used during breastfeeding only if the potential benefits to the mother outweigh the potential risks, including those to the breastfed child.

Driving a vehicle or performing other hazardous tasks
Enterogermina® has no influence on the ability to drive and use machines.

Undesirable effects
The following CIOMS frequency rating is used, when applicable:
Very common ≥10%; Common ≥ 1 and <10%; Uncommon ≥0.1 and <1%;
Rare ≥ 0.01 and < 0.1%; Very rare< 0.01%; Not known (cannot be estimated from available data).

Skin and subcutaneous tissue disorders:
During post marketing experience, hypersensitivity reactions, including rash, urticaria and angioedema have been reported.

Infections and infestations:
Not known: Bacteremia, septicemia or sepsis in immunocompromised patients or those hospitalized due to a serious illness.

Overdose
No cases of overdose have been reported.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties
Pharmacotherapeutic category: antidiarrhoeal microorganisms
Enterogermina® is a preparation consisting of a suspension of 4 spore strains (SIN, O/C, T, N/R) of *Bacillus clausii,* which naturally occur in the intestine and is non-pathogenic.

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When administered orally, Bacillus clausii spores cross, thanks to their high resistance to both chemical and physical agents, cross the barrier of the acidic gastric juice, reaching the intestinal tract unharmed, and there they are transformed into metabolically active vegetative cells. Spores can survive heat and gastric acidity, by nature. In a validated in vitro model, *Bacillus clausii* spores demonstrated to survive in a simulated gastric environment (pH 1.4-1.5) until 120 minutes (survival rate of 96%). In a model that simulates the intestinal environment (saline solution of bile and pancreatin - pH 8), Bacillus clausii spores demonstrated their capability to multiply compared to the initial amount, in a statistically significant way (from 109 to 1012 CFU – Colony-Forming Units), starting from 240 minutes after incubation.
In a study that was conducted in 20 individuals, it was noticed that in humans, *Bacillus Clausii* spores persist in the intestine and can be found in faeces until 12 days after a single oral administration.

The administration of Enterogermina® contributes to the restoration of intestinal microbial flora that is altered by dysmicrobism, also known as dysbiosis, that results from the antibiotic therapy and that can be associated with gastrointestinal symptoms, e.g. diarrhoea, abdominal pain and increased air in the intestine.
In two open randomized controlled clinical trials, Enterogermina® demonstrated to reduce the duration of acute diarrhoea in children older than 6 months.
When taken during the antibiotic treatment and the next 7- 10 days, Enterogermina® demonstrated to reduce the incidence of abdominal pain and diarrhoea that are associated with antibiotic treatment.

A prospective, observational, multicentre study conducted on 261 patients evaluated the 'real-world' use of the probiotic *Bacillus clausii* for symptoms such as diarrhoea, pain, bloating, meteorism, constipation and abdominal tension through the administration of a questionnaire by the pharmacist before starting to take it and after 30 days.
Patients reported taking the medicinal product mainly for diarrhoea (56.7%), abdominal pain (13.41%) and bloating (12.64%). The mean duration of treatment was 7.1 days. On average, the improvement in symptoms was perceived after it had been taken for 3 days. After treatment, 95% of patients reported an improvement in diarrhoea and 97% an improvement in abdominal pain.

The 2 main mechanisms, reported below, contribute to Bacillus clausii effect of restoring the intestinal bacterial flora.

Growth Inhibition of Pathogenic Bacteria
The three *B. clausii* supposed mechanisms of action are: colonization of free ecological niches, thatare made unavailable by the growth of other microorganisms; competition for the bond with epithelial cells, that is particularly relevant for the spores in the germination initial and intermediate phases; production of antibiotics and/or enzymes that are secreted in the intestinal environment. In an in vitro study, *Bacillus clausii* spores demonstrated to produce bacteriocins and antibiotics such as clausin, with antagonist activity against Gram-positive bacteria - *Staphylococcus aureus, Clostridium difficile, Enterococcus faecium.*

Immunomodulatory activity
Bacillus clausii spores, administered through oral route, in in vitro and in vivo murine models demonstrated to stimulate the production of Interferon-gamma and to increase the CD4+ T Lymphocyte proliferation.
Furthermore, Bacillus clausii demonstrated itscapability of producing various B vitamins, aiding in correcting avitaminosis due to intestinal bacterial flora.
Furthermore, the high level of artificially induced heterologous resistance to antibiotics creates the therapeutic conditions for preventing the alteration of the intestinal microbial flora, by the selective action of antibiotics, particularly broad- spectrum antibiotics, or for restoring the intestinal microbial flora.
Due to its antibiotic resistance, Enterogermina® may be administered between two subsequent administrations of antibiotics.
Antibiotic resistance refers to: penicillins, if not in combination with beta-lactamase inhibitors, cephalosporins (partial resistance in most cases), tetracyclines, macrolides, aminoglycosides (except for gentamicin and amikacin), chloramphenicol, thiamphenicol, lincomycin, clindamycin, isoniazid, cycloserine, novobiocin, rifampicin, nalidixic acid and pipemidic acid (intermediate resistance), metronidazole.

PHARMACEUTICAL PARTICULARS

List of excipients
Purified water Ph. Eur

Incompatibilities
None

Storage
Do not store above 30 °C.
KEEP OUT OF THE REACH OF CHILDREN.

Instructions for use
Shake the mini bottle before use. After mini bottle has been opened, the preparation should be taken shortly to avoid any contamination of the suspension.
For oral use only. Do not inject.

Manufactured by:
Opella Healthcare Italy s.r.l., Viale Europa, 11 - 21040 - Origgio (VA) – Italy

Importer:
Opella Healthcare India Private Limited, Building No. B-4, Gala No.2, First Floor, City Link Warehouse Complex, NH3, Vadape Village, Bhiwandi Thane, Taluka: Mumbai Nashik Highway (NH3) (Thane-Zone2), Maharashtra, Pin: 421302.

Source:
1. Bacillus clausii CCSI v3 LRC dated 12th March 2020
2. Italian SmPC dated August 2024

Updated: January 2025

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940444 - IST ENTEROG 2MLD/5ML BT10 M24 IN

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Reason for artwork pdf approval	Electronically signed by	Date
Market regulatory validation	Disha Dhairyawan (India Regulatory team)	07/07/2025 13:21:18
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