

Bacipore

(Bacillus clausii spores)

Anti-diarrheal

2 Billion/5 ml & 4 Billion/5ml Oral Suspension

COMPOSITION

2 Billion / 5 ml:

Each ampoule contains:

Probiotic Spores Bacillus clausii $\geq 2 \times 10^9$ CFU

(Innovator's Specs.)

4 Billion / 5 ml:

Each ampoule contains:

Probiotic Spores Bacillus clausii $\geq 4 \times 10^9$ CFU

(Innovator's Specs.)

THERAPEUTIC INDICATIONS

Treatment and prevention of intestinal dysmicrobism and subsequent endogenous avitaminosis.

Coadjuvant treatment to restore the intestinal microbial flora, altered during treatment with antibiotics or chemotherapy. Acute and chronic gastrointestinal disorders in infants, attributable to poisoning or intestinal dysmicrobism and avitaminosis.

DOSAGE AND METHOD OF ADMINISTRATION

Adults: 2-3 ampoule per day.

Children: 1-2 ampoule per day. **Infants:** 1-2 ampoule per day.

Ampoule: administration at regular intervals. Take the ampoule content as it is or dilute it in water or other beverages (e.g., milk, tea, orange juice). This medication is for oral use only. Do not inject or administer in any other way.

CONTRAINDICATIONS

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

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Special warnings

Any presence of visible corpuscles in the ampoule of Bacillus clausii spores is due to aggregates of Bacillus clausii spores; it does not therefore suggest that the product has been altered.

Shake the ampoule before use.

This medicinal product is for oral use only. Do not inject or administer in any other way.

Incorrect use of the medicinal product has caused severe anaphylactic reactions such as anaphylactic shock.

Precautions for use

During treatment with antibiotics, it is recommended that the preparation be administered between antibiotic administrations.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed.

FERTILITY, PREGNANCY AND LACTATION

There are no contraindications for use of the preparation during pregnancy or lactation.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Bacillus clausii spores has no influence on the ability to drive and use machines.

UNDESIRABLE EFFECTS

Skin and subcutaneous tissue disorders:

Unknown frequency: hypersensitive reactions, including rash, hives and angioedema.

Infections and infestations:

Unknown frequency: bacteraemia (in immunocompromised patients)

REPORTING OF SUSPECTED ADVERSE REACTIONS

Reporting suspected adverse reactions via: pv@searlecompany.com

OVERDOSE

No cases of overdose have been reported.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics properties

Pharmacotherapeutic Category: Antidiarrheal microorganisms

ATC CODE: A07FA

Bacillus clausii spores is a preparation consisting of a suspension of 4 strain (SIN, O/C, T, N/R) spores of Bacillus clausii, which occurs naturally in the intestine and non-pathogenic. When administered orally, Bacillus clausii spores, 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 the incubation. In a study that was conducted on 20 individuals, it was noticed that, in humans, Bacillus clausii spores persist in the intestine and can be found in feces until 12 days after a single oral administration.

The administration of Bacillus clausii spores 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. diarrhea, abdominal pain and increase of air in the intestine.

In two open randomized controlled clinical trials, Bacillus clausii spores demonstrated to reduce the duration of acute diarrhea in children older than 6 months.

When taken during the antibiotic treatment and the next 7-10 days, Bacillus clausii spores

demonstrated to reduce the incidence of abdominal pain and diarrhea that are associated with the antibiotic treatment.

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, that are 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 the 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 its capability of producing various B vitamins, aiding in correcting avitaminosis due to intestinal bacterial flora imbalance.

Furthermore, the high level of artificially induced heterologous resistance to antibiotics creates the therapeutic conditions for preventing the alteration of 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, *Bacillus clausii* spores 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 piperidic acid (intermediate resistance), metronidazole.

PRESENTATION

Bacipore 2Billion/5ml ampoules are available in pack of 10's (1x10's).

Bacipore 4Billion/5ml ampoules are available in pack of 10's (1x10's).

Enlistment NUMBER

Company Enlistment Number	:	01438
Bacipore 2Billion/5ml Ampoule	:	014381220064
Bacipore 4Billion/5ml Ampoule	:	014381220063

INSTRUCTIONS:

To be sold on the prescription of a registered medical practitioner only.

Protect from sunlight, moisture and heat.

Do not store and transport above 30°C.

Keep all medicines out of sight & reach of children.

Note: For detailed information please refer to SPC available on website www.searlecompany.com

Manufactured by:

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Manufactured by:

Manufactured For:
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SPL/SMPC- BAC.S./724-000(001)