

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ENTEROL® 250

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Saccharomyces boulardii CNCM I-745..... 250.00 mg
(lyophilized cells of *Saccharomyces boulardii* CNCM I-745)

Excipient with known effect: lactose, fructose, sorbitol (contained in tutti-frutti aroma)

For the full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension in sachets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

ENTEROL 250 is indicated for the prevention and treatment of diarrhea of different etiologies in adults and children, such as:

- Symptomatic treatment of diarrhoea
- Prevention of antibiotic-induced diarrhoea
- Prevention of diarrhoea, e.g. when travelling
- Addition to vancomycin/metronidazole treatment to prevent recurrence of *Clostridium difficile*-induced diarrhoea

4.2. Posology and method of administration

Posology

New-born: not more than 1 sachet per day under supervision, strictly follow the advises of your physician.

Children under 6 years: 1 sachet 1-2 times per day

Adults and children over 6 years old: 1-2 sachets 2 times per day.

Recommended period of treatment:

Short-term symptomatic treatment of diarrhoea: for one week.

Prevention of antibiotic-induced diarrhoea:

Treatment should be started within 48 to 72 hours of the beginning of treatment with antibiotics and it should continue for at least three days and not longer than four weeks after the treatment with antibiotics is ended.

Prevention of diarrhoea e.g. when travelling:

Treatment should be started couple of days before travelling and should be continued as long as travelling.

Addition to vancomycin/metronidazole treatment to prevent recurrence of Clostridium difficile-induced diarrhoea: Treatment should be started as soon possible after the beginning of antibiotic treatment and it should continue for 4 weeks.

Method of administration

Pour the contents of the sachet in a little water or sweetened beverage, mix, and drink. The powder can also be mixed with food or poured into a baby's feeding-bottle. It should not be poured or mixed with very cold or very hot liquids or food nor alcoholic drinks.

Due to a risk of airborne contamination, sachets should not be opened in patient rooms. Healthcare providers should wear gloves during handling of probiotics for administration, then promptly discard the gloves and properly wash their hands (see section 4.4).

4.3. Contra-indications

- Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1.;
- Patient with central venous catheter (see section 4.4).
- Immunocompromised or hospitalised patients (due to serious illness or altered/weakened immune system).

4.4. Special warnings and special precautions for use.

Special warnings

If symptoms persist for more than 2 days of treatment at usual posology, the therapeutic approach will be reevaluated.

The treatment does not replace rehydration when this is necessary. The rehydration dose and its route of administration (oral-IV) should be adapted to the severity of the diarrhoea and to the age and state of health of the patient.

There have been very rare cases of fungaemia (and blood cultures positive for *Saccharomyces* strains) and sepsis reported mostly in patients with central venous catheter, critically ill or immunocompromised patients, most often resulting in pyrexia. In most cases, the outcome has been satisfactory after cessation of treatment by *Saccharomyces boulardii*, administration of antifungal treatment and removal of the catheter when necessary. However, the outcome was fatal in some critically ill patients (see section 4.3 and 4.8).

As with all medicines made from living micro-organisms, special attention must be paid to the handling of the product in the presence of patients mainly with central venous catheter but also with peripheral catheter, even not treated with *Saccharomyces boulardii*, in order to avoid any contamination by hands and/or spread of microorganisms by air (see section 4.2).

It is advisable not to open the sachets in the surroundings of patients with a central venous catheter, to avoid any colonization, especially hand-borne, of the catheter. There have been reports in patients with a central venous catheter, even not treated with *S. boulardii*, of very rare cases of fungemia (penetration of blood by yeast), most often resulting in pyrexia and blood cultures positive for *Saccharomyces*. The outcome in all these cases has been satisfactory after administration of antifungal treatment and, when necessary, removal of the catheter.

ENTEROL 250 mg, powder for oral suspension contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicine.

ENTEROL 250 mg, powder for oral suspension contains fructose: Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

ENTEROL 250 mg, powder for oral suspension contains sorbitol.

This medicine contains 0,10 mg sorbitol in each sachet. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

Precautions for use

The patients must be told of the need:

- to rehydrate themselves by drinking copious amounts of salty or sweet drinks, in order to compensate for fluid losses due to diarrhea (mean daily water requirement of an adult is 2 liters);
- to eat while they have diarrhea: excluding certain types of food and especially raw salads, fruit, green vegetables, spicy foods and iced foods or drinks, and preferring grilled meats and rice.

Since ENTEROL 250 consists of living cells that develop at 37°C: do not mix it with a liquid or food which is too hot (more than 50°C), iced or containing alcohol.

4.5. Interaction with other drugs and other forms of interaction

Because of its fungal nature, ENTEROL 250 must not be administered with systemic or oral antifungal drugs. No other interaction is expected.

4.6. Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

There are no reliable animal teratogenesis data. Clinically, no malformative nor foetotoxic effect has been reported to date. However, monitoring of pregnancies exposed to this medicine is insufficient to rule out any risk.

As a precautionary measure, ENTEROL 250 is not recommended during pregnancy.

Lactation

Saccharomyces boulardii CNCM I-745 is not absorbed. In the normal conditions of use, this medicine can be taken during breast-feeding.

4.7. Effects on ability to drive and use machines

ENTEROL 250 has no influence on the ability to drive or use machines.

4.8. Side effects

The side effects which have been reported are classified hereafter by system-organ class and by frequency defined by: very common ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1,000$, $< 1/100$), rare ($\geq 1/10,000$, $< 1/1,000$), very rare ($< 1/10,000$, including isolated cases) and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing severity.

System/organ classes

System Organ Class (MedDRA terminology)	Rare	Very rare	Unknown
Gastrointestinal disorders	Flatulence		constipation

System Organ Class (MedDRA terminology)	Rare	Very rare	Unknown
Skin and subcutaneous tissue disorders		Allergic reactions: pruritus, wheal formation (urticaria), skin rash, either locally restricted or affecting the entire body (local or generalized exanthema), swelling of the connective tissue of the face (angioedema).	
Immune system disorders		Anaphylactic reaction or even shock	
Infections and infestations		Fungemia in patients with a Central venous catheter and critically ill or immunocompromised patients (see section 4.4)	Sepsis in critically ill or immunocompromised patients (see section 4.4)

4.9. Overdose

No case has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ANTI-DIARRHOEA, microorganism

Replacement flora

Pharmacotherapeutic group: A, digestive system and metabolism, ATC code: A07FA02

Saccharomyces boulardii CNCM I-745 is an intestinal flora replacement which acts as antidiarrheal microorganisms in the digestive tract.

Pharmacodynamics of *Saccharomyces boulardii* CNCM I-745, live probiotic cultures, have been established on various models by *in vitro* and *in vivo*, animal, and human studies which demonstrated it has:

- anti-inflammatory (enterohemorrhagic *E. Coli*) effect,
- anti-microbial (enterohemorrhagic *E. Coli*; *C. difficile*; *S. typhimurium*; *Yersinia enterocolitica*; *C. albicans*; *C. krusei*; *C. pseudotropicalis*) effect,
- enzymatic (disaccharidases; leucine aminopeptidase; spermine; spermidine) effect,
- metabolic effect,
- anti-toxin (*C. diff.* toxin A; cholera toxin) effect,
- and immuno-enhancing (secretory-IgA and immunoglobulins) effect

which are beneficial when *Saccharomyces boulardii* CNCM I-745 is used to treat diarrhea of various origins (infectious -viral, bacterial- or not) in humans.

5.2. Pharmacokinetic properties

Saccharomyces boulardii CNCM I-745 is not absorbed. After repeated oral doses, it transits in the digestive tract without colonizing it, rapidly attaining significant intestinal concentrations which are maintained at a constant level throughout the administration period. *Saccharomyces boulardii* CNCM I-745 is no longer present in the stools 2 to 5 days after discontinuation of treatment.

5.3. Preclinical safety data

LD50 is much higher than the maximal administered dose of 3,000 mg/kg – repeated dose toxicity has been tested for 6 months in rats and 6 weeks in rabbits without any damage for animals.

An Ames test has been performed and no mutagenic effect has been observed. There is no available data on reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1. Excipients

Lactose monohydrate, fructose, colloidal anhydrous silica, tutti frutti flavor (Flavouring substances, maltodextrin (maize), sorbitol syrup E420, gum arabic/acacia gum E414, butylated hydroxyanisole E320, methyleugenol, safrol).

6.2. Incompatibilities

None

6.3. Shelf-life

3 years.

6.4. Special precautions for storage

Keep this medicine out of the sight and reach of children.

Do not use after the expiry date which is stated on the carton.

Store at a temperature below 25°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6.5. Nature and contents of container

Packaged in twin sachets. Each sachet consists in a paper/aluminum foil/polyethylene film, containing 765 mg of a very light-brown powder with an odor of fruit.

Box of 10 sachets.

7. MANUFACTURER AND MARKETING AUTHORISATION HOLDER

Manufacturer address

BIOCODEX

1 avenue Blaise Pascal
60000 BEAUVAIS
France

Marketing Authorization Holder

BIOCODEX

22 Rue des Aqueducs
94250 GENTILLY
France

8. MARKETING AUTHORISATION NUMBER

N 21508

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

April 29th, 2002

10. DATE OF REVISION OF THE TEXT

March 2025

CONDITIONS OF PRESCRIPTION AND DISPENSING

Without medical prescription.