SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ENTEROL® 250

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Saccharomyces boulardii CNCM I-475 ..... 250.00 mg
(lyophilized cells of *Saccharomyces boulardii* CNCM I-745)
to one capsule.

Excipient with known effect: lactose.
For the full list of excipients: see section 6.1

3. PHARMACEUTICAL FORM

Capsule.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

ENTEROL 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

Adults and children over 6 years old: 1-2 capsules 1-2 times per day. For children below 6 years old, use the powder for oral suspension more adapted for small children.

APPROVED BIOMEDICINE JSC
EXPERT/DATA 23.02.18
APPLICANT/DATA 26.02.18

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.

Always take this medicine exactly as described in this leaflet or as your pharmacist has told you.
The capsules must be swallowed with a little water.
Administering capsules is contraindicated in children under 6 years old, as there is risk of aspiration. For this age group, Enterol oral powder will be administered.

The lyophilisation of the active substance guarantees the good stability and vitality of *Saccharomyces boulardii*.

4.3. Contra-indications

- Hypersensitivity to the active ingredient or to any of the components listed in section 6.1.
- Patients with central venous catheter (see section 4.4).

4.4. Special warnings and 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.

It is advisable not to open capsules 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.

Because of the presence of lactose, this medicine is contra-indicated in patients suffering from congenital galactosemia, glucose and galactose malabsorption syndrome or lactase deficit.

Precautions for use

APPROVED BY SCIENTE JSC
EXPERT/DATA 23.02.18
APPLICANT/DATA 26.02.18

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 diarrhoea: 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 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 must not be administered with oral or systemic 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. Therefore, as a precaution, it is not recommended to take this medicine during pregnancy.

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

4.8. Undesirable effects

The side effects which have been reported are classified hereafter by system-organ class and by frequency defined by: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000, < 1/100), rare (≥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**
Gastrointestinal disorders	Flatulence	
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

4.9. Overdose

No case of overdose has been reported.

APPROVED BY SCIENTE JSC
CONFIDENTIAL 23.02.18
CONFIDENTIAL 26.02.18

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 yeast, 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 enterolitica*; *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* 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, magnesium stearate
Composition of the capsule shell: gelatin, titanium dioxide (E171).

APPROVED BY SCONTE JSC
EXPERT/DATA 23.02.18
APPLICANT/DATA 26.02.18

6.2. Incompatibilities

None.

6.3. Shelf-life

3 years.

6.4. Special precautions for storage

Stay away from light at a temperature below 25°C.

6.5. Nature and contents of container

The capsules are presented in type III glass bottle with LDPE stopper.

7. MARKETING AUTHORISATION HOLDER

BIOCODEX
7 avenue Gallieni
94250 GENTILLY
France

APPROVED BY SCIENTIFIC ISC
23.02.18
APPLICATION DATA 26.02.18

8. MARKETING AUTHORISATION NUMBER

N 12305

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

April 29th, 2002

10. DATE OF REVISION OF THE TEXT

October 2017

CONDITIONS OF PRESCRIPTION AND DISPENSING

Without medical prescription.