ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BIOFLOR® 250mg, capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

- Treatment of acute infectious (viral or bacterial) diarrhea.
- Preventive and curative treatment of antibiotic-associated diarrhea and colitis.
- Preventive treatment of recurrence of *Clostridium difficile* disease in addition to vancomycin/metronidazole.
- Preventive treatment of tube-feeding associated diarrhea.
- Treatment of irritable bowel syndrome.

BIOFLOR 250mg, capsule is indicated in adults and children above 6 years of age.

4.2. Posology and method of administration

Posology

1 or 2 capsules once or twice daily.

Method of administration

Oral route.
Swallow the capsules with a glass of water.
In young children under 6 years of age, it is recommended not to swallow capsules (risk of false passage) and to use the powder for oral suspension in sachet.

Due to a risk of airborne contamination, capsules 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 substance or to any of the excipients listed in section 6.1.
- Patients with central venous catheter (see section 4.4).
- Critically ill patients or immunocompromised patients due to a risk of fungaemia (see section 4.4).

4.4. Special warnings and precautions for use

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

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) 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 sections 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 the spread of microorganisms by air (see section 4.2).

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.

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, fruits, green vegetables, spicy foods and iced foods or drinks, and preferring grilled meats and rice.

Since BIOFLOR 250mg, capsule 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 medicinal products and other forms of interaction
Because of its fungal nature, BIOFLOR 250mg, capsule must not be administered with oral or systemic antifungal drugs.

4.6. Fertility, pregnancy and lactation
Pregnancy
There are no reliable animal teratogenesis data.
There have been no clinical reports to date of any malformative or fetotoxic effect. However, the monitoring of pregnancies exposed to this medicine is insufficient to rule out any risk. Hence, as a precautionary measure, this medicine should not be used during pregnancy.

Breast-feeding
Due to the absence of data about the excretion of this drug in breast milk, the use of it has to be avoided during breast-feeding.

4.7. Effects on ability to drive and use machines
Not relevant.

4.8. Undesirable effects
The side effects which have been reported are classified hereafter by system-organ class and by frequency defined as: 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) and not known (cannot be estimated from the available data).
Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

System Organ Class (MedDRA terminology)	**Rare**	**Very rare**	**Not known**
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	
Gastrointestinal disorders	Flatulence		Constipation
Infections and infestations		Fungemia in patients with a central venous catheter and in critically ill or immunocompromised patients (see section 4.4)	

4.9. Overdose
No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Anti-diarrhoea. Replacement flora.
ATC code: A07FA02. (A: Digestive system and metabolism).

5.2. Pharmacokinetic properties
After repeated oral doses, *Saccharomyces boulardii* CNCM I-745 transits in the digestive tract without colonizing it.
S. boulardii CNCM I-745 quickly disappears from stools 2 to 5 days after treatment is stopped.

5.3. Preclinical safety data
There is no animal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Lactose, magnesium stearate
Composition of the capsule shell: gelatin, titanium dioxide (E 171).

6.2. Incompatibilities
Not applicable.

6.3. Shelf-life
3 years.

6.4. Special precautions for storage
Store away from humidity at a temperature below 25°C.

6.5. Nature and contents of container
Glass bottle with polyethylene cap.
Box of 10 capsules.

6.6. Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

FDA/SD.173-121170

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th December 2017

10. DATE OF REVISION OF THE TEXT

January 2019