1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S0

1. NAME OF THE MEDICINE

INTEFLORA SACHETS powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of INTEFLORA SACHETS contains 250 mg lyophilised cells of *Saccharomyces boulardii*

CNCM I-745.

Contains sugar:

Fructose: 471,90 mg per sachet

Lactose monohydrate 32,5 mg per sachet

Sorbitol 0,11 mg per sachet

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sachets

A very light brown powder with an odour of fruit.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

INTEFLORA SACHET has been used for:

- Diarrhoea associated with antibiotic therapy.

- Non-specific acute diarrhoea.

Suitable for use in infants, children, adults and in the elderly.

4.2 Posology and method of administration

May be taken in conjunction with antibiotics and other anti-diarrhoeal medication.

Length of treatment can range from 1 week to 3 weeks.

Diarrhoea associated with antibiotic therapy

Adults: Take two sachets twice a day.

Non-specific acute diarrhoea

Adults: Take one sachet twice a day.

Paediatric population

Diarrhoea associated with antibiotic therapy

Infants and children: Give one sachet twice a day.

Non-specific acute diarrhoea

Infants and children: Give one sachet twice a day.

Method of administration

For oral administration.

Pour the contents of the sachet(s) in a little amount of water or sweetened beverage, mix and drink immediately (see section 4.4). 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 Contraindications

INTEFLORA SACHET is contraindicated in:

- Patients with a known hypersensitivity to any component contained in INTEFLORA SACHET (see sections 2 and 6.1).
- Patients with a central venous catheter *in situ*.
- Critically ill patients or immunocompromised patients due to risk of fungaemia (see section 4.4).
- Because of the presence of lactose, this medicine is contraindicated in patients with congenital galactosaemia, glucose and galactose malabsorption syndrome or lactase deficiency (see section 4.4).
- Because of the presence of fructose and sorbitol, this medicine is contraindicated in patients with fructose intolerance (see section 4.4).
- Patients taking alcohol.
- Patients taking oral or systemic antifungal medicines (see section 4.5).

4.4 Special warnings and precautions for use

INTEFLORA SACHET should not be opened in close proximity of patients with a venous central catheter or with a peripheral catheter, even not treated with *Saccharomyces boulardii* to avoid any colonisation of the catheter, transmitted by the hands and/or the spread of microorganisms by air (see section 4.2 Method of administration).

There have been 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 sections 4.3 and 4.8).

In infants and children, if diarrhoea persists after 2 days of treatment, treatment must be reviewed and the need for rehydration using an oral or intravenous solution envisaged. Diarrhoea may be a symptom of a more serious underlying disease. If diarrhoea persists for more than 2 days, or there is blood in stools, or fever develops, treatment should be reconsidered.

In infants, children and adults be aware of the following:

1. Rehydration by drinking copious amounts of salty or sweet drinks is recommended, in order to compensate for fluid losses due to diarrhoea.
2. INTEFLORA SACHET should not be used concomitantly with antifungals (see sections 4.3 and 4.5).
3. Since INTEFLORA SACHET consist of living cells, do not mix the content of INTEFLORA SACHET with liquid or food which are too hot (more the 50 °C), iced or contains alcohol (see sections 4.2 and 4.3).

Therefore INTEFLORA SACHET should not be used concomitantly with hot beverages, ice cream and alcohol (see section 4.2 and 4.3).

Excipients

INTEFLORA SACHET contains lactose, fructose and sorbitol.

Patients with hereditary fructose intolerance (HFI), rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take INTEFLORA SACHET.

4.5 Interaction with other medicines and other forms of interaction

Because of its fungal nature, do not combine INTEFLORA SACHET with an oral or systemic antifungal medication (see section 4.3).

4.6 Fertility, pregnancy and lactation

Safety of INTEFLORA SACHET in pregnancy and lactation has not been established.

Pregnancy

It is preferable, as a precautionary measure, not to use this medicine during pregnancy.

Lactation

It is preferable, as a precautionary measure, not to use this medicine during lactation.

Fertility

No data.

4.7 Effects on ability to drive and use machines

INTEFLORA SACHET is not expected to influence on the ability to drive and use machines as *Saccharomyces boulardii* CNCM I-745, as contained in INTEFLORA SACHET, is not absorbed into the blood.

4.8 Undesirable Effects

a) *Tabulated list of adverse reactions*

System organ class	Rare	Very rare	Unknown
Infections and infestations		Fungemia in patients with a central venous catheter, and in hospitalised, immunocompromised patients (see section 4.4).	Sepsis in critically ill or immunocompromised patients
Immune system disorders		Anaphylactic reaction or even shock	
Gastrointestinal disorders	Flatulence		Constipation
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).	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Saccharomyces boulardii CNCM I-745 is not absorbed into the blood circulation and any overdose is merely excreted via the gastrointestinal tract.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

A 11.9.2 Antidiarrhoeals, other

Pharmacotherapeutic group: Antidiarrheal microorganisms

ATC code: A07FA02

Mechanism of action

Acute infectious diarrhoeas result from a disruption of the gastrointestinal ecosystem thus favouring the colonization by enteropathogens and promoting their ability to upset the enterosystemic water cycle. Thus along with specific antidiarrhoeal medication, there should also be active rehydration of the patient.

INTEFLORA SACHET contains a living yeast, *Saccharomyces boulardii* CNCM I-745, which is active in the gastrointestinal tract. This yeast has an antagonistic effect against the overgrowth of different enteropathogenic bacteria (*Shigella dysenteriae, Salmonella typhi, Escherichia coli*) and *Candida albicans*.

It also enhances non-specific immune defences in the case of experimental bacterial (*Staphylococcus aureus, Salmonella enteritidis)* or fungal (*Candida albicans*) invasions. These actions re-establish the equilibrium of the gastrointestinal ecosystem and so reduce diarrhoea.

Saccharomyces boulardii CNCM I-745 also synthesizes and supplies vitamin B components within the gastrointestinal tract. This yeast is genetically resistant to antibacterial medicines and so can be taken in conjunction with antibiotics to prevent diarrhoea (see section 4.2).

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica, artificial tutti frutti flavour.

Lactose monohydrate, fructose, sorbitol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C, protect from moisture.

Keep in the original packaging.

6.5 Nature and contents of container

Packed in cartons of 10 sachets.

The product is packed in 5 twin sachets consisting of paper/aluminum foil/polyethylene film composite.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8 REGISTRATION NUMBER

44/11.9.2/0783

9 DATE OF FIRST AUTHORISATION

23 November 2017

10 DATE OF REVISION OF TEXT

Date of last Pharmaceutical and Analytical revision: 07 June 2020

Date of last Clinical revision: 31 March 2023

INTEFLORA is a registered trademark of Biocodex SAS.

ZA_INTEPWD_2303_00