BIOCODEX

7 avenue Gallieni
94250 GENTILLY - FRANCE

28/12/2017

Direct Healthcare Professional Communication on the New contra-indication for *Saccharomyces boulardii* in critically ill or immunocompromised patients

Dear Healthcare professional,

Biocodex in agreement with Malta Medicines Authority would like to inform you of the following:

Summary

- There have been rare cases of fungaemia in patients receiving *Saccharomyces boulardii* including fatal cases in critically ill patients.
- Bioflor capsules and sachets are now contraindicated in critically ill or immunocompromised patients. These products were already contraindicated in patients with a central venous catheter.
- Other patients who are in close proximity to patients being treated with *S. boulardii* may also be at risk of contamination with the microorganisms. Therefore, special attention must be paid to the handling of the product in the presence of critically ill or immunocompromised patients or patients with central venous catheter or peripheral catheter who are not treated with *S. boulardii*.
- To avoid any hand-borne or air-borne contamination with the microorganisms, sachets or capsules should not be opened in patient rooms. Healthcare providers should wear gloves during handling of probiotics and then promptly discard the gloves and properly wash their hands.

Background on the safety concern

S. boulardii is an intestinal replacement flora available as a lyophilised product derived from a cultured yeast strain.

S. boulardii is indicated for adjuvant symptomatic treatment of diarrhoea in addition to rehydration and/or dietetic measures and (in some countries) also for prophylaxis and treatment of antibiotic-associated diarrhoea and recurrence of *Clostridium difficile* disease (CDD) in addition to vancomycin and metronidazole.

The risk of fungaemia in patients with central venous catheter is already known. Rare cases of fungaemia have now been reported in hospitalised critically ill or immunocompromised patients (also without central venous catheter), most often resulting in pyrexia. In most cases of fungaemia, the outcome has been satisfactory after cessation of treatment with *S. boulardii*, administration of antifungal treatment and removal of the catheter when necessary. However, the outcome was fatal in some critically ill patients.

Therefore the product information (Summary of Product Characteristics and Package Leaflet) for *S. boulardii* products is being updated to include a new warning and contraindication.

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Call for reporting

Any suspected adverse drug reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form available online at http://www.medicinesauthority.gov.mt/adrportal and sent to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point

Suspected adverse reactions to *Saccharomyces boulardii* may also be reported to Biocodex: vigilance@biocodex.fr. Tel: +33 1 40 24 30 00.

Annex I

The following changes to the product information of medicinal products containing the active substance *Saccharomyces boulardii* are approved:

- Section 4.2 Posology and method of administration

Due to a risk of airborne contamination, sachets or 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).

- Section 4.3 Contraindications

Known hypersensitivity to one of the components; allergy to yeast, especially *Saccharomyces boulardii*; patients having a central venous catheter; **critically ill patients or immunocompromised patients due to a risk of fungaemia (see section 4.4).**

- Section 4.4 Special warnings and precautions for use

There have been very rare cases of fungaemia (and blood cultures positive for *Saccharomyces* strains) reported mostly in patients with central venous catheter and critically ill or immunocompromised patients, most often resulting in pyrexia. In most cases, the outcome has been satisfactory after cessation of treatment with *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).

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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 hand and/or the spread of microorganisms by air (see section 4.2).

- Section 4.8 Undesirable effects

System Organ Class	**Rare**	**Very rare**
Infections and infestations		Fungaemia in patients with a central venous catheter **and in critically ill or immunocompromised patients (see section 4.4)**