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### ABRIDGED PRESCRIBING INFORMATION:

**Composition:** Each sachet of BIOGIT® contains *Saccharomyces boulardii* 250 mg, lactose 40 mg, D-Fructose 497.5 mg, colloidal silica 7.5 mg, Artificial flavour 5 mg. **Description:** *Saccharomyces boulardii* is a live, non-pathogenic yeast recommended as a probiotic and as a biotherapeutic in the treatment of diarrhoea of various etiology. BIOGIT® is a creamy white powder with brown coloured granules. **Indications:** For acute gastroenteritis or acute infectious diarrhoea, and antibiotic associated diarrhoea.<sup>23</sup> For diarrhoea during continuous enteral feeding in adults only.

**Dosage & Administration:** Adults & Children, 1-2 sachets twice daily, or as directed by the physician. BIOGIT® should be taken orally, directly or mixed with water or beverage. It should not be mixed in hot liquids or liquids which contain alcohol. BIOGIT® can be taken before or after food. For continuous enteral feeding, the drug may be added to the nutrient solution at the time of preparation.

**Contraindications:** Known hypersensitivity to any of the ingredients of the formulation. Patients with central venous catheter. Pregnancy and lactation. Because of the fungal nature of this formulation it should not be administered with systemic or oral antifungal drugs.

**Side-effects:** Various clinical trials with *Saccharomyces boulardii* and post-marketing surveillance studies have not shown any significant side-effects. Occasionally, a temporary increase in digestive gas is known to occur. **Storage:** In cool, dry place. Keep out of reach of children.

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## DIARRHOEA - LEADING KILLER IN YOUNG CHILDREN<sup>1</sup>



Diarrhoea kills 2,195 children every day - more than AIDS, Malaria, and Measles combined.

1 in 9 child deaths worldwide occurs due to diarrhoea, making it the 2<sup>nd</sup> leading cause of mortality in children under 5 years of age.

## MORTALITY DUE TO DIARRHOEA IN INDIA<sup>2</sup>



India contributes significantly to the global burden. 3<sup>rd</sup> leading cause of childhood mortality.

13% of all-cause mortality in children under 5 years of age.

**Most diarrhoeal deaths are preventable using simple & effective low cost interventions.**

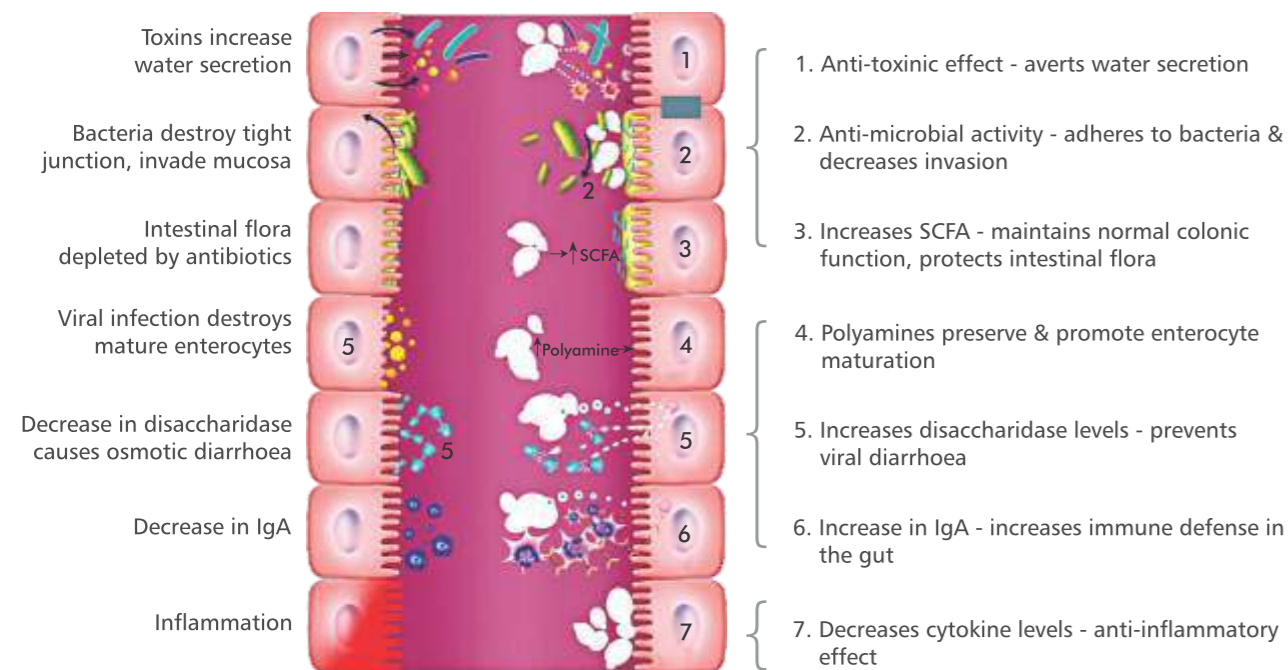
### BIOGIT® (SACCHAROMYCES BOULARDII) - SALIENT FEATURES

- India's 1<sup>st</sup> DCGI\* approved probiotic yeast.
- Manufactured in stringent, world-class GMP facility.
- Assured 5 billion live yeast per sachet.
- Granular form, highly palatable & specially designed for children.
- Assured high quality with nitrogen flushed Alu-Alu pack.
- Unlike FSSAI<sup>†</sup> approved food products, BIOGIT™ is therapeutic grade product.

### SACCHAROMYCES BOULARDII (S. BOULARDII) FOR DIARRHOEA<sup>3</sup>

- S. boulardii is a non-pathogenic probiotic.
- It has a unique ability to survive in varied gut environment.
- Proven to be stable, highly effective when co-administered with antibiotics unlike lactic acid bacillus.
- Eukaryotic probiotic, hence preferred choice for antibiotic-induced diarrhoea.

### S. BOULARDII - MECHANISM OF ACTION (MOA)<sup>4</sup>



SCFA, Short Chain Fatty Acids, \*DCGI: Drug Controller General of India; <sup>†</sup>FSSAI: Food Safety and Standards Authority of India.

## PUBLISHED STUDIES ON S. BOULARDII IN ACUTE DIARRHOEA

Various published studies authenticate effectiveness of S. boulardii treatment outcomes

Authors	Age-group & Conditions	Results
Cetina-Sauri et al. <sup>5</sup> (1994) Mexico	<ul style="list-style-type: none"> <li>130 children</li> <li>3 months - 3 years</li> <li>Acute watery diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>The endpoint of cure of acute diarrhoea was 85% in the S. boulardii group vs 40% in placebo.</li> </ul>
Castaneda Guillot et al. <sup>6</sup> (1995) Cuba	<ul style="list-style-type: none"> <li>40 children</li> <li>6 - 36 months</li> <li>Chronic diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>70% of the patients in the S. boulardii group showed a highly significant improvement, with only 10% improvement in the placebo group.</li> </ul>
Hafeez et al. <sup>7</sup> (2002) Pakistan	<ul style="list-style-type: none"> <li>101 children</li> <li>6 - 60 months</li> <li>Acute watery diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>The average duration of illness was 3.6 days in S. boulardii group compared with 4.5 days in controls.</li> </ul>
Kurugöl et al. <sup>8</sup> (2005) Turkey	<ul style="list-style-type: none"> <li>200 children</li> <li>3 months - 7 years old</li> <li>41.5% rotavirus</li> <li>Shigella flexneri (n=5), Salmonella (n=4), Amebiasis (n=6), Giardia (n=3), Cryptosporidium (n=3)</li> <li>Acute diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>Duration of hospital stay was shorter in the S. boulardii group (2.9 vs 3.9 days, p&lt;0.001).</li> </ul>
Ozkan et al. <sup>9</sup> (2007) Turkey	<ul style="list-style-type: none"> <li>27 children</li> <li>6 months - 10 years</li> <li>Acute diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>Significant increase in serum IgA with S. boulardii therapy.</li> </ul>
Villarruel et al. <sup>10</sup> (2007) Argentina	<ul style="list-style-type: none"> <li>88 children (72 children evaluated at first month)</li> <li>3 - 24 months</li> <li>Acute diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>The total duration of diarrhoea significantly reduced in the S. boulardii group vs placebo (4.7 vs 6.16 days; p&lt;0.05).</li> </ul>
Vandenplas et al. <sup>11</sup> (2007) Indonesia and India	<ul style="list-style-type: none"> <li>188 children</li> <li>3 - 33months</li> <li>Acute diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>The duration of diarrhoea was 66.57±52.52h in the control group vs 53.65±38.74h (difference ~13h or 20% of duration) in the S. boulardii group (p&lt;0.05).</li> </ul>
Htwe et al. <sup>12</sup> (2008) Myanmar	<ul style="list-style-type: none"> <li>100 children</li> <li>3 months - 10 years (89%, 3 months - 2 years)</li> <li>Acute watery diarrhoea</li> <li>21% Escherichia coli</li> </ul>	<ul style="list-style-type: none"> <li>The mean duration of diarrhoea was shorter in the S. boulardii group than placebo (3.0 vs 4.7 days; p&lt;0.05).</li> </ul>
Correa et al. <sup>13</sup> (2011) Brazil	<ul style="list-style-type: none"> <li>176 children</li> <li>6 - 48 months</li> <li>Acute diarrhoea 72h before hospitalization</li> <li>57.4% rotavirus positive</li> </ul>	<ul style="list-style-type: none"> <li>The beneficial effect of S. boulardii was observed especially in rotavirus cases (persistent diarrhoea in 29.2 vs 64.4%) of patients compared in patients with non-rotaviral diarrhoea (persistent diarrhoea in 41.2 vs 54.3%).</li> </ul>
Riaz et al. <sup>14</sup> (2011) India	<ul style="list-style-type: none"> <li>3 - 59 months</li> <li>Acute diarrhoea (admitted less than 48h of onset)</li> <li>14/93 rotavirus positive</li> </ul>	<ul style="list-style-type: none"> <li>The mean post-intervention duration of diarrhoea was significantly shorter in the S. boulardii group (52.08 ± 24.57 vs 64.04 ± 30.43 hours).</li> </ul>
Burande et al. <sup>15</sup> (2013) India	<ul style="list-style-type: none"> <li>72 Children</li> <li>3 months - 24 months</li> <li>Acute diarrhoea</li> </ul>	<ul style="list-style-type: none"> <li>Average time of recovery for the study group was 2.5 ± 1.2 days vs 3.3 ± 1.2 days for control group</li> </ul>
Das et al. <sup>16</sup> (2016) India	<ul style="list-style-type: none"> <li>3 months - 5 years</li> <li>Acute watery diarrhoea and stool rotavirus positive (n=60)</li> </ul>	<ul style="list-style-type: none"> <li>Median duration of diarrhoea was significantly shorter in the S. boulardii group (60 vs 89 hours).</li> </ul>

## S. BOULARDII IN ANTIBIOTIC-ASSOCIATED DIARRHOEA (AAD)<sup>17</sup>

- S. boulardii reduced risk of AAD from 18.7% to 8.5% when compared with placebo or no treatment groups.
- In children, S. boulardii reduced the AAD risk from 20.9% to 8.8%.
- Analyses showed a reduction in the risk of diarrhoea associated with antibiotic treatment, regardless of the reason for which the antibiotics were used.

### PUBLISHED STUDIES ON S. BOULARDII IN ANTIBIOTIC-ASSOCIATED DIARRHOEA

Authors	Age-group & Conditions	Results
Erdeve et al. <sup>18</sup> (2004) Turkey	<ul style="list-style-type: none"> <li>466 children receiving sulbactam-ampicillin and azithromycin</li> </ul>	<ul style="list-style-type: none"> <li>In the group receiving sulbactam-ampicillin, use of S. boulardii decreased the diarrhoea rate from 32.3% to 11.4% in the 1-5 years age group.</li> </ul>
Kotowska et al. <sup>19</sup> (2005) Poland	<ul style="list-style-type: none"> <li>6 months - 14 years</li> <li>N=269</li> </ul>	<ul style="list-style-type: none"> <li>S. boulardii reduced the risk of AAD caused by Clostridium difficile or otherwise unexplained diarrhoea (3.4% vs 17.3%).</li> </ul>
Biloo et al. <sup>20</sup> (2006) Pakistan	<ul style="list-style-type: none"> <li>100 children</li> <li>2 months - 12 years</li> </ul>	<ul style="list-style-type: none"> <li>S. boulardii reduced the no. of episodes of diarrhoea by 50% in the subsequent 2 months.</li> </ul>
Shan et al. <sup>21</sup> (2013) China	<ul style="list-style-type: none"> <li>333 hospitalised children</li> </ul>	<ul style="list-style-type: none"> <li>Diarrhoea prevalence was lower in S. boulardii group plus antibiotics than in antibiotics only group (7.9% vs 29.2%).</li> </ul>
Basnet et al. <sup>22</sup> (2017) Nepal	<ul style="list-style-type: none"> <li>174 children with respiratory tract infections</li> </ul>	<ul style="list-style-type: none"> <li>Diarrhoea occurred in 12.6% of the patients in the amoxicillin and clavulanate group vs 1.1% of the patients in amoxicillin and clavulanate plus S. boulardii group.</li> </ul>

### GUIDELINES<sup>23</sup>

Guidelines	Acute gastroenteritis, Treatment	Antibiotic-associated diarrhoea, Prevention
European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe, 2014	✓	✓
The use of probiotics in pediatric gastroenterology: a review of the literature and recommendations by Latin American experts, 2015	✓	✓
World Gastroenterology Organisation Global Guidelines, Probiotics and Prebiotics, 2017	✓	✓
Probiotics for gastrointestinal disorders: proposed recommendations for children of the Asia-Pacific region, 2017	✓	✓