VISBIOME® (De Simone Formulation) High Potency Probiotic.

Live, lyophilized, probiotic cultures for oral administration.

VISBIOME medical food, as defined by the Orphan Drug Act. Physician supervision is required. VISBIOME is not an FDA-approved drug.

Contains the same formulation found in VSL#3®† produced before January 31, 2016 (the "De Simone Formulation"). After January 2016 the VSL#3® product was changed. The sellers were ordered by a U.S. court to stop any claims that state or suggest a false continuity between the new formulation sold as VSL#3® and the original De Simone Formulation.

VISBIOME contains the original De Simone Formulation.

†VSL#3® is a registered trademark of VSL Pharmaceuticals, Inc.

----------RECENT MAJOR CHANGES----------

Warnings and Precautions	10/2021
Dairy Status	10/2021
Dosing Intake	06/2023
Name Changes	09/2023
GI Care Inactive Ingredients/labeling	10/2023
Advanced GI Care Inactive Ingredients/labeling	01/2024
Extra Strength GI Care Ingredients/labeling	01/2024

----------INTENDED USE----------

VISBIOME is a probiotic medical food intended for the dietary management of dysbiosis associated with:

- Irritable Bowel Syndrome (IBS)
- Ulcerative Colitis (UC)
- Antibiotic-associated diarrhea (AAD)
- Hepatic Encephalopathy (HE)
- Ileal Pouch Management

VISBIOME is a non-drug therapy that addresses distinct nutritional requirements to promote microbial balance in individuals which cannot be addressed by modification of the diet alone. VISBIOME is intended to be used under the supervision of a physician.

---------DOSAGE AND ADMINISTRATION----------

VISBIOME GI CARE CAPSULES (Formerly VISBIOME CAPSULES):

- VISBIOME GI CARE CAPSULES can be consumed directly or pulled apart and sprinkled on cold food. Adjustment of the intestinal flora can take a few days or weeks.

VISBIOME ADVANCED GI CARE PACKETS (Formerly VISBIOME UNFLAVORED):

- Can be mixed into 3-6 oz cold water or any cold, non-carbonated beverage, blended into a smoothie, or mixed into foods such as yogurt or apple sauce, and consumed promptly.
- Stir or shake contents until mixed.
- Promptly consume all contents (mixture may settle on the bottom of glass over time).
- Do not mix with hot food or drinks.
- Adjustment of the intestinal flora can take a few days or weeks. It may take up to one month to colonize the gut to become optimally stable when consumed regularly.

VISBIOME EXTRA STRENGTH GI CARE PACKETS (Formerly VISBIOME EXTRA STRENGTH):

- Dispensed by medical food prescription.
- Can be mixed into 3-6 oz cold water or any cold, non-carbonated beverage, blended into a smoothie, or mixed into foods such as yogurt or apple sauce, and consumed promptly.
- Stir or shake contents until mixed.
- Promptly consume all contents (mixture may settle on the bottom of glass over time).
- Do not mix with hot food or drinks.
- Adjustment of the intestinal flora can take a few days or weeks. It may take up to one month to colonize the gut to become optimally stable when consumed regularly.

----------DOSAGE FORMS AND STRENGTHS---------

VISBIOME is available in three (3) dosage forms:

- VISBIOME GI CARE CAPSULES - 112.5 billion (112.5×10^9) Colony Forming Units (CFUs) per capsule. Inactive ingredients: microcrystalline cellulose (derived from plant fiber) vegetable capsule (hydroxypropyl methylcellulose).
- VISBIOME ADVANCED GI CARE PACKETS - 450 billion (450×10^9) CFUs per packet. Inactive ingredients: maltose.
- VISBIOME EXTRA STRENGTH GI CARE PACKETS - 900 billion (900×10^9) CFUs per packet. Inactive ingredients: maltose.

----------CONTRAINDICATIONS----------

VISBIOME should not be used in premature infants in the Neonatal Intensive Care Unit (NICU) setting.

----------WARNINGS AND PRECAUTIONS----------

VISBIOME contains milk. Some milk components are used as a fermentation nutrient. Trace amounts of dehydrated skim milk powder or milk protein may be present in the product.

Lactose Status – VISBIOME is Lactose-free: Lactose was not detectable in amounts greater than 50 parts per million (PPM).

----------ADVERSE REACTIONS----------

Mild abdominal bloating has been occasionally reported during the first few days of consuming VISBIOME. This is generally associated with a readjustment of the microbiota, which usually diminishes within 3-4 days. If bloating persists, the patient should reduce their intake for a few days and consult with their healthcare provider.

To report SUSPECTED ADVERSE REACTIONS, contact EXEGI PHARMA, LLC at 1-844-FIT-GUTS (1-844-348-4887) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or *www.fda.gov/medwatch*

----------DRUG INTERACTIONS----------

There are no known adverse drug interactions associated with the consumption of VISBIOME. The bacteria in VISBIOME may be inactivated by certain antibiotics. When taking an antibiotic with VISBIOME, consume the antibiotic four (4) hours before or four (4) hours after taking VISBIOME.

----------USE IN SPECIFIC POPULATIONS----------

The probiotic formulation in VISBIOME has been the subject of studies in adults, children, and infants. If you are pregnant or nursing, please consult with your healthcare provider before consuming VISBIOME.

FULL PRESCRIBING INFORMATION: CONTENTS

FULL PRESCRIBING INFORMATION

1. INTENDED USE

1.1 VISBIOME is a probiotic medical food intended for the dietary management of dysbiosis associated with:

- Irritable Bowel Syndrome (IBS)
- Ulcerative Colitis (UC)
- Antibiotic-Associated Diarrhea (AAD)
- Hepatic Encephalopathy (HE)
- Ileal Pouch Dietary Management

VISBIOME is a non-drug therapy that addresses distinct nutritional requirements to promote microbial balance in individuals which cannot be addressed by modification of the diet alone. VISBIOME is intended to be used under the supervision of a physician.

1.2 VISBIOME is intended for the clinical dietary management of patients who, because of therapeutic or chronic medical needs, have special medically determined nutrient requirements; the dietary management of which cannot be achieved by the modification of the normal diet alone.

VISBIOME, as a medical food, must be used under physician supervision.

VISBIOME EXTRA STRENGTH GI CARE is a medical food, which is dispensed by a medical food prescription.

2. DOSAGE AND ADMINISTRATION

FOR ORAL ADMINISTRATION:

VISBIOME GI CARE CAPSULES (Formerly VISBIOME CAPSULES): Each capsule contains at least 112.5 billion (112.5×10^9) colony-forming units (CFUs).

Consume 1-4 capsules daily. as directed by your healthcare provider. VISBIOME GI CARE Capsules can be consumed directly. Adjustment of the intestinal flora can take a few days or weeks; it may take up to one month for the colonization of the gut to become optimally stable if consumed regularly.

VISBIOME ADVANCED GI CARE PACKETS (Formerly VISBIOME UNFLAVORED POWDER): Each packet contains at least 450 billion (450×10^9) colony-forming units (CFUs).

Consume one (1) to two (2) packets daily as directed by your healthcare provider. It can be mixed into 3-6 oz of cold water or any cold, non-carbonated beverage, blended into a smoothie, or mixed into foods such as yogurt or apple sauce, and consumed promptly. Adjustment of the intestinal flora can take a few days or weeks; it may take up to one month for the colonization of the gut to become optimally stable when consumed regularly.

VISBIOME EXTRA STRENGTH GI CARE PACKETS (Formerly VISBIOME EXTRA STRENGTH POWDER): Each packet contains at least 900 billion (900×10^9) colony-forming units (CFUs).

Consume one (1) to two (2) packets daily as directed by your physician. VISBIOME EXTRA STRENGTH GI CARE can be mixed into 3-6 oz cold water or any cold, non-carbonated beverage, blended into a smoothie, or mixed into foods such as yogurt or apple sauce, and consumed promptly. Adjustment of the intestinal flora can take a few days or weeks; it may take up to one month for the colonization of the gut to become optimally stable if consumed regularly.

2.1 ADULT ADMINISTRATION-

Medical Food Applications			
	Irritable Bowel Syndrome 1 – 4 GI Care Capsules Daily 112.5 - 450 Billion	**Advanced Irritable Bowel Syndrome** 1 Advanced GI Care Packet Daily 450 Billion	**Advanced Ulcerative Colitis** 1 Extra Strength GI Care Packets Daily 900 Billion
	Antibiotic-Associated Diarrhea During Antibiotic Treatment 4 GI Care Capsules Daily 450 Billion After Antibiotic Treatment 2 GI Care Capsules Daily 225 Billion (for at least 10 days)	**Ulcerative Colitis** 1-2 Advanced GI Care Packets Daily 450-900 Billion	**Ileal Pouch Management** 1-2 Extra Strength GI Care Packets Daily 900-1800 Billion
	Hepatic Encephalopathy 2-4 GI Care Capsules Daily 225-450 Billion		

2.1.1 Visbiome GI Care Capsules, Visbiome Advanced GI Care Powder Packets, and Visbiome Extra Strength GI Care Powder Packets:

** Each Capsule Contains 112.5 Billion Live Bacteria (Colony Forming Units -CFUs).*
***Each Advanced GI Care Packet Contains 450 Billion Live Bacteria (Colony Forming Units -CFUs).*
****Each Extra Strength GI Care Packet Contains 900 Billion Live Bacteria (Colony Forming Units-CFUs).*

2.2 PEDIATRIC ADMINISTRATION-

For the Dietary Management of:	Irritable Bowel Syndrome (IBS)	Advanced Irritable Bowel Syndrome (IBS)	Ulcerative Colitis (UC)
2-5 Years	1 GI Care Capsule Daily Pull apart the capsule and sprinkle on food. 112.5 Billion	2 GI Care Capsules Daily Pull apart capsules and sprinkle on food. 225 Billion	½ Advanced GI Care Powder Packet Daily 225 Billion
6-11 Years	1-2 GI Care Capsules Daily Pull apart capsules and sprinkle on food. 112.5-225 Billion	1 Advanced GI Care Powder Packet Daily 450 Billion	1 Advanced GI Care Powder Packet Daily 450 Billion
12-17 Years	1-4 GI Care Capsules Daily 112.5-450 Billion	1 Advanced GI Care Powder Packet Daily 450 Billion	1-2 Advanced GI Care Powder Packets Daily 450-900 Billion

3. DOSAGE FORMS AND INGREDIENTS

3.1 DOSAGE FORMS:

VISBIOME is a powder consisting of eight (8) strains of live, lyophilized, probiotic bacteria. VISBIOME is available in three (3) dosage forms:

- VISBIOME GI CARE CAPSULES (Formerly VISBIOME CAPSULES)- 112.5 billion CFUs per capsule. 60 capsules per bottle. Inactive ingredients: microcrystalline cellulose (derived from plant fiber) and vegetable capsules (hydroxypropyl methylcellulose).
- VISBIOME ADVANCED GI CARE PACKETS (Formerly VISBIOME UNFLAVORED PACKETS) - 450 billion CFUs per packet. 30 packets per carton. Inactive ingredients: maltose.
- VISBIOME EXTRA STRENGTH GI CARE PACKETS (Formerly VISBIOME EXTRA STRENGTH PACKETS) -900 billion CFUs per packet. 30 packets per carton. Inactive ingredients: maltose.

3.2 INGREDIENTS:

VISBIOME contains the De Simone Formulation, a proprietary blend of the following live, lyophilized, probiotic bacteria:

Genus	Species	Deposit Reference
Lactobacillus	*acidophilus*	DSM24735/SD5212
Lactobacillus	*plantarum*	DSM24730/SD5209
Lactobacillus	*paracasei*	DSM24733/SD5218
Lactobacillus	*delbrueckii* subsp. *bulgaricus*†	DSM24734/SD5210
Bifidobacterium	*longum*±	DSM24736/SD5219
Bifidobacterium	*breve*	DSM24732/SD5206
Bifidobacterium	*infantis*±	DSM24737/SD5220
Streptococcus	*thermophilus*	DSM24731/SD5207

[*]Reclassified as Bifidobacterium lactis
[†]Reclassified as Lactobacillus helveticus

4. CONTRAINDICATIONS

VISBIOME should not be used in premature infants in the Neonatal Intensive Care Unit (NICU) setting.

5. WARNINGS AND PRECAUTIONS

Contains milk. Some milk components are used as a fermentation nutrient in product processing. Trace amounts of dehydrated skim milk powder or milk protein may be present in the finished product.

Allergens:

The table below indicates the presence (as an added component) of the following allergens and products thereof:

Yes	No	Allergen	Description
	X	Wheat	
	X	Other cereals containing gluten	
	X	Crustacean shellfish	
	X	Eggs	
X		Corn	The maltose in the VISBIOME Advanced GI Care and VISBIOME Extra Strength GI Care may contain trace amounts of corn
	X	Fish	
	X	Peanuts	
	X	Soybeans	
X		Milk	Used as fermentation nutrient
	X	Nuts/Tree Nuts	
	X	Celery	
	X	Mustard	
	X	Sesame seeds	
	X	Sulfur dioxide and sulfites (> 10 mg/kg)	
	X	Lupine	

6. ADVERSE REACTIONS

Mild abdominal bloating has been occasionally reported during the first few days of consuming VISBIOME. This is generally the result of a readjustment of the microbiota, which usually diminishes within 3-4 days. If bloating persists, the patient should reduce their intake for a few days and consult with their healthcare provider.

7. DRUG INTERACTIONS

There are no known adverse drug interactions associated with consumption of VISBIOME. Some strains of bacteria in VISBIOME may be inactivated by certain antibiotics. When taking an antibiotic with VISBIOME, consume the antibiotic four (4) hours before or four (4) hours after taking VISBIOME.

8. USE IN SPECIFIC POPULATIONS

The probiotic formulation in VISBIOME has been the subject of studies in adults, children, and infants. If you are pregnant or nursing, please consult with your healthcare provider before consuming VISBIOME.

9. SAFETY AND OVERDOSAGE

Probiotics have a long history of safe use, having been consumed for health benefits and as part of fermented foods for

millennia.[1,2,3,4] Many bifidobacteria and lactobacilli species are normal, non-pathogenic inhabitants of the human gastrointestinal tract, oral cavity, skin, and vagina.[1,2,5,6] Documented cases of infection attributable to probiotic intake are limited to individual case reports, primarily associated with the use of probiotics in severely immunocompromised patients. VISBIOME has been the subject of clinical trials in ART-treated HIV-1 positive patients.[9,10,7]

The probiotic bacteria in VISBIOME are non-pathogenic, non-toxigenic, and Generally Recognized as Safe (GRAS) as food ingredients.

The De Simone Formulation in VISBIOME has been the subject of over 80 clinical studies involving over 5,000 adults, children, and infants - including immunocompromised individuals.[8,9,10] The most common reported adverse events are abdominal bloating and/or gas, generally reported within the first few days of probiotic consumption.

VISBIOME has been administered in clinical evaluation in daily dosages of up to 3,600 billion (3,600 x 10^9) CFUs per day for 12 weeks.

10. MEDICAL FOOD STATUS

The Orphan Drug Act of 1988 defines "medical food" as "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation" 21 U.S.C. 360ee(b)(3). FDA regulations 21 C.F.R. 101.9(j)(8) set forth additional criteria for makers of medical food products.

VISBIOME is a medical food as defined by the Orphan Drug Act and additional FDA regulations. VISBIOME is specially formulated and processed to provide a precise mixture of certain bacterial species to the gastrointestinal tract. The gastrointestinal microbiota, or "microbiome", is important for the normal functioning of the human gastrointestinal tract.[11,12,13] Healthy gut microbes compete with pathogens for nutrients and adhesion sites on the gut mucosa.[14] The gut microbiome also plays a critical role in human digestion with key probiotic bacteria being essential for the fermentation of non-digestible fibers.[15] Fermentation of non-digestible fibers results in the production of short-chain fatty acids such as butyrate which is a critical energy source for human colonic cells. Additionally, the gut microbiome plays a role in modulating intestinal inflammation and improving gut barrier function.[16]

Patients who experience irritable bowel syndrome (IBS), ulcerative colitis (UC), and an ileal pouch anastomosis often have documented dysbiosis associated with limited bacterial diversity and deficiencies in luminal concentrations of lactobacilli and bifidobacteria compared with healthy individuals.[17,18,19,20,21,22] Likewise, the consumption of antibiotics can have a dramatic short and long-term impact on the healthy gut microbiome with reductions in bacterial evenness and diversity at phylum and species levels.[23,24,25,26] And finally, the gut microbiome of patients with hepatic encephalopathy (HE) has also been shown to be significantly altered compared to healthy controls with significant increases in ammonia-producing bacterium present and other differences in bacterial species compared to controls.[27,28,29,30,31,32]

Patients with dysbiosis associated with these gastrointestinal and liver disorders have distinct nutritional requirements that differ from the general population, and which require the consumption of high levels of probiotic bacteria to maintain an adequate and balanced microbiota. While alterations in the normal diet can impact the microbiome, there is insufficient evidence to suggest that, in these patient groups, adjustment of the microbiota can be achieved through modification of the normal diet alone.

VISBIOME is intended for those who are receiving active and ongoing medical supervision with regular instruction on the use of medical foods.

11. CLINICAL DATA – Exclusive to the De Simone Formulation

In the 1990's, Professor Claudio De Simone invented and patented a number of multi-strain probiotic formulations with specific biochemical and immunologic profiles. One of these formulations – the De Simone Formulation – was licensed to VSL Pharmaceuticals, Inc. ("VSL Inc") and was subsequently produced under the brand name, "VSL#3®*" from 2002 to January 31, 2016. When De Simone terminated his relationship with VSL Inc., he partnered with ExeGi Pharma, LLC to market his De Simone Formulation under the brand, VISBIOME. Therefore, clinical trials cited in this package insert were performed with the De Simone Formulation and are applicable to the evaluation of VISBIOME as a medical food.

VISBIOME contains the same formulation found in VSL#3* produced before January 31, 2016 (the "De Simone Formulation") - An imitation of the original De Simone Formulation was launched in 2016 under the name VSL#3. In 2019, an injunction was issued by the U.S Federal Court for the District of Maryland preventing the makers of new VSL#3 from citing the historical clinical data on the original formulation as though these studies had been performed on their new product.[33] VISBIOME contains the original De Simone Formulation.

11.1 Clinical Experience - Irritable Bowel Syndrome (IBS) Dietary Management

The De Simone Formulation has been the subject of over 80 published clinical trials in human subjects, with extensive clinical research in the dietary management of dysbiosis associated with irritable bowel syndrome (IBS), ulcerative colitis (UC), ileal pouch management, hepatic encephalopathy (HE), and antibiotic-associated diarrhea (AAD). VISBIOME is a medical food and not an FDA-approved drug product.

The De Simone Formulation has been the subject of over ten clinical trials involving over 550 adult and pediatric patients in the dietary management of dysbiosis associated with IBS.[34,35,36,37,38,39,40,41,42,43,73] In one study, 25 patients with diarrhea-predominant IBS received the De Simone Formulation or a placebo for eight weeks. Patients receiving the De Simone Formulation as a medical food experienced a statistically significant reduction in abdominal bloating.[35] In a second study, 48 patients with Rome II IBS were randomized in a double-blind design to the probiotic or placebo. Patients receiving the De Simone Formulation medical food experienced a statistically significant reduction in flatulence ($p=0.01$).[34] The De Simone Formulation was well tolerated with no adverse events reported in either IBS studies.

11.2 Clinical Experience - Ulcerative Colitis (UC) Dietary Management

The De Simone Formulation has been the subject of published clinical studies in ulcerative colitis involving nearly 500 adult and 47 pediatric patients.[44,45,46,47,48,49,66,67] In these studies, daily consumption of the De Simone Formulation was associated with effective dietary management of ulcerative colitis.

In one study involving 90 adult patients, the De Simone Formulation plus low-dose balsalazide was compared to balsalazide, or mesalamine alone in the dietary management of acute ulcerative colitis. The De Simone Formulation plus low-dose balsalazide was superior to balsalazide or mesalamine alone in achieving dietary management of remission (85.7% vs. 80.8% vs. 72.7%; $p<0.02$), with improved time to remission (4 days vs. 7.5 vs. 13; $p<0.001$). In a second study involving 34 adult patients with acute UC, dietary management with the De Simone Formulation resulted in a combined 77% remission/response rate with no adverse effects, as measured by UCDAI score (53% remission, 24% response).[49]

In the dietary management of UC, the De Simone Formulation was also shown to help achieve remission when added to standard therapies (mesalazine, azathioprine, or 6-mercaptopurine). In a multicenter, randomized, double-blind, placebo-controlled trial (n=147) patients consuming the De Simone Formulation had significantly higher remission rates vs. placebo (43% vs. 16%; $p< 0.001$). In the same study, UCDAI scores for patients consuming the De Simone Formulation showed a significant decrease by 50% from baseline ($p<0.001$).[47]

The European Society for Clinical Nutrition and Metabolism (ESPEN) recognizes the De Simone Formulation as one of two probiotics that should be considered as a dietary aid in the maintenance of remission and induction of remission in patients with ulcerative colitis.[50,51]

11.3 Clinical Experience – Antibiotic-Associated Diarrhea (AAD)

In a double-blind, randomized, controlled clinical trial, 229 hospitalized patients on systemic antibiotics were administered the De Simone Formulation probiotic or placebo. Patients were administered a variety of antibiotics in intravenous and oral formulations, including penicillin's, broad-spectrum penicillin's, cephalosporins, quinolones, macrolides, aminoglycosides, imidazole's, and others. The probiotic or placebo was administered within 48 hours of the first hospital antibiotic treatment. The rate of AAD was significantly lower in the active group vs placebo on a per-protocol analysis (0% active vs 11.4% placebo; $p=0.006$).[52]

11.4 Clinical Experience – Ileal Pouch Dietary Management

In three double-blind, placebo-controlled trials and one open trial, the De Simone Formulation has been shown to help with the management of the ileal pouch.[53,54,55,68] The formulation found in VISBIOME is recognized as a tool for ileal pouch management by the American College of Gastroenterology,[56] the European Society of Clinical Nutrition and Metabolism[57] the British Society of Gastroenterology,[57] the Asian Working Group[59] and The Cochrane Collaboration.[58]

11.5 Clinical Experience - Hepatic Encephalopathy (HE) Dietary Management

In the dietary management of dysbiosis associated with hepatic encephalopathy (HE), the De Simone Formulation has been the subject of multiple controlled clinical studies involving over 800 patients.[61,62,63,64, 65] In one placebo-controlled trial involving 160 patients with cirrhosis, those consuming the De Simone Formulation for dysbiosis experienced a reduced incidence of HE, reduced ammonia levels, and improvements in psychometric tests compared to controls. Seven patients in the probiotic group experienced overt HE vs. 14 patients in the control group ($p<0.05$).[65]

In a second study, 235 patients with cirrhosis who had prior episodes of HE were evaluated after consuming the De Simone Formulation, lactulose, or no therapy. There was a significant difference in the development of HE in the probiotic vs. no treatment group ($p=0.02$) and in the lactulose vs. no treatment group ($p=0.001$), but no difference between the probiotic group vs. lactulose ($p=0.134$).[62]

11.6 Clinical Experience – Pediatric Ulcerative Colitis (UC) Dietary Management

The De Simone Formulation was the subject of two trials involving patients between the ages of 1.7 and 17 years of age with active ulcerative colitis (UC). In one trial, 29 patients were randomized to receive dietary management with the De Simone Formulation or placebo concomitantly with standard UC treatment (steroids, 5-ASA). Thirteen patients (92.8%) of those supplemented with the De Simone Formulation and standard therapy achieved remission vs. four patients (36.4%) in the placebo arm ($p<0.001$). In addition, 21.4% of patients consuming the De Simone Formulation and standard UC therapy and 73.3% of patients consuming placebo and standard therapy relapsed within 1 year of follow-up ($p=0.014$). At six months, 12 months, or at the time of relapse, endoscopic and histological scores were lower in the probiotic group than in the placebo group.[66]

In a second study, the De Simone Formulation was administered open-label for eight weeks in pediatric patients with mild to moderate acute UC. Ten patients (56%) achieved remission and the combined remission/response rate was 61%.[46]

The De Simone Formulation was studied in 59 pediatric IBS patients, aged 4 to 18 years old, diagnosed with IBS using the Rome II criteria. The group who was administered the De Simone Formulation as a medical food had statistically significant improvements in the primary endpoint of subjective assessment of relief of symptoms ($p<0.05$) and the secondary endpoints of abdominal pain/discomfort ($p<0.05$), abdominal bloating/gassiness ($p<0.01$), and family assessment of life disruption. However, there were no significant changes in stool pattern.[38]

11.7 Clinical Experience – Pediatric Irritable Bowel Syndrome (IBS) Dietary Management

The De Simone Formulation was studied in 59 pediatric IBS patients, aged 4 to 18 years old, diagnosed with IBS using the Rome II criteria. The group who was administered the De Simone Formulation as a medical food had statistically significant improvements in the primary endpoint of subjective assessment of relief of symptoms ($p<0.05$) and the secondary endpoints of abdominal pain/discomfort ($p<0.05$), abdominal bloating/gassiness ($p<0.01$), and family assessment of life disruption. However, there were no significant changes in stool pattern.[38]

12. PRODUCT INFORMATION - STORAGE AND HANDLING

- VISBIOME GI CARE CAPSULES (Formerly Visbiome Capsules) consist of 112.5 x 10^9 (112.5 billion) probiotic bacteria per capsule – 60 Capsules.
- VISBIOME ADVANCED GI CARE PACKETS (Formerly Visbiome Unflavored Packets) consists of 450 x 10^9 (450 billion) probiotic bacteria per packet – 30 Packets.
- VISBIOME EXTRA STRENGTH GI CARE PACKETS (Formerly Visbiome Extra Strength Packets) consists of 900 x 10^9 (900 billion) probiotic bacteria per packet – 30 Packets.
- VISBIOME contains a proprietary blend of live, lyophilized, probiotic bacteria:
    - *Lactobacillus acidophilus* DSM24735/SD5212
    - *Lactobacillus plantarum* DSM24730/SD5209
    - *Lactobacillus paracasei* DSM24733/SD5218
    - *Lactobacillus delbrueckii* subsp. *bulgaricus*† DSM24734/SD5210
    - S*treptococcus thermophilus* DSM24731/SD5207
    - *Bifidobacterium longum*± DSM24736/SD5219
    - *Bifidobacterium breve* DSM24732/SD5206
    - *Bifidobacterium infantis*± DSM24737/SD5220
- VISBIOME is partially soluble in water.
- VISBIOME is shipped and stored cold to ensure maximum potency (36 - 46° F / +2 - +8° C). Do not freeze.
- VISBIOME can be stored at room temperature for up to one week without adversely impacting potency.

±Reclassified as Bifidobacterium lactis
†Reclassified as Lactobacillus helveticus

Product Version	Product Code	Carton Size
VISBIOME GI CARE CAPSULES	69355-0412-03	60 capsules per bottle
VISBIOME ADVANCED GI CARE PACKETS	69355-0412-02	30 packets per carton
VISBIOME EXTRA STRENGTH GI CARE PACKETS	69355-0516-01	30 packets per carton

VISBIOME contains the following inactive ingredients:

- VISBIOME GI CARE CAPSULES - Inactive ingredients: microcrystalline cellulose (derived from plant fiber) and vegetable capsule (hydroxypropyl methylcellulose).
- VISBIOME ADVANCED GI CARE PACKETS - Inactive ingredients: maltose.
- VISBIOME EXTRA STRENGTH GI CARE PACKETS - Inactive ingredients: maltose.

13. DAIRY, LACTOSE, GMO, GLUTEN, HALAL, KOSHER, FODMAP STATUS

- **Dairy Status** - VISBIOME contains milk. Some milk components are used as a fermentation nutrient. Trace amounts of milk protein may be present in the finished product.
- **Lactose Status** - VISBIOME is lactose-free (not detectable in amounts greater than 50 PPM).
- **GMO Status** - VISBIOME is non-GMO.
- **Gluten Status** - VISBIOME is gluten-free.
- **Halal Status -** VISBIOME is Halal suitable.
- **Kosher Status** -VISBIOME is Kosher certified.
- **FODMAP Status -** Low-FODMAP certified by Monash University.

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