For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

VIZYLAC GG DROPS

1. Generic name

Lactobacillus rhamnosus GG Drops (ATCC 53103)

2. Qualitative and quantitative composition

Each dosage (7 drops/0.25ml) contains:

Lactobacillus rhamnosus GG Drops……1 Billion CFU
(ATCC 53103)

Ingredients: Medium chain triglyceride oil, *Lactobacillus rhamnosus* GG Drops (ATCC 53103), Anticaking agent (INS 551), Antioxidant (INS 307).

No added flavours or colours.

3. Dosage form and strength

Lactobacillus rhamnosus GG Drops……1 Billion CFU

4. Clinical particulars

4.1. Therapeutic indication

- Probiotic Food
- For restoration of intestinal microflora

4.2. Posology and method of administration

Direction for use: Shake the bottle well until the suspended materials are dispersed. Remove the cap. Tilt the bottle at about 45° angle to release 7 drops in a spoon. Do not administer directly from the bottle into the mouth or add hot milk or food.

To be given only under medical advice by physician/ certified dietician/ nutritionist for children below 5 years.

7 drops per day before or after the first meal or as directed by healthcare professionals.

Use within 14 days from the date of opening under recommended storage condition; discard the unused material after 16 days. Keep the bottle closed.

Nutritional Information:

Serving size: 7 drops (Apx 0.25ml)	Apx Qty. per serving	%RDA*
Energy (Kcal)	2.097	0.40
Protein (g)	0.002	0.03
Carbohydrate	0.009	-
Of which sugars (g)	0	-
Total Fats (g)	0.228	-
Of which saturated fat (g)	0.224	-
Trans-fat (g)	0	-
Cholesterol (mg)	0	-
Sodium (mg)	0.003	-

*Calculated for 0-6 months

4.3 Contraindications

- There are no absolute contraindications to probiotics comprised of *Lactobacillus* sp. But some may have an allergies to *Lactobacillus rhamnosus*.
- There are typically few or no adverse effects; flatulence or mild abdominal discomfort, usually self-limited, are reported occasionally. There have been reports of pathologic infection, including bacteremia with probiotic species following oral administration. These are rare, occurring in severely ill or immunocompromised hosts, or in children with shortgut syndrome. It is prudent to avoid probiotics in these patients, or to be aware of the risk of sepsis. A recently reported systematic review, examined the safety of *L. rhamnosus* GG and *Bifidobacterium*sp and concluded that the risk of sepsis is low, with no cases reported in any prospective clinical trial. There are no reports of sepsis or other pathologic colonization in healthy patients. There are also no known interactions with medications or other supplements.

4.4 Special warnings and precautions for use

Warning:

- Not to exceed the stated recommended daily usage. Avoid contact of the in-dropper with saliva or water.
- Keep out of reach of children.
- Not for medicinal use.
- Trans-Fat Free
- Before using this product, tell the doctor or pharmacist if you are allergic to it; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to pharmacist for more details.

Precautions:

If you have any of the following health problems, consult the doctor or pharmacist before using this product: diarrhea lasting more than 2 days (especially if you also have a high fever), weakened immune system (such as due to chemotherapy, HIV infection), recurring vaginal infections, recurring urinary tract infections.

4.5 Drugs interactions

Antibiotic drugs interact with *LACTOBACILLUS*

Antibiotics are used to reduce harmful bacteria in the body. Antibiotics can also reduce friendly bacteria in the body. Lactobacillus is a type of friendly bacteria. Taking antibiotics along with lactobacillus can reduce the effectiveness of lactobacillus. To avoid this interaction, take lactobacillus products at least 2 hours before or after antibiotics.

Medications that decrease the immune system (Immunosuppressants) interacts with *LACTOBACILLUS*

Lactobacillus contains live bacteria and yeast. The immune system usually controls bacteria and yeast in the body to prevent infections. Medications that decrease the immune system can increase your chances of getting sick from bacteria and yeast. Taking lactobacillus along with medications that decrease the immune system might increase the chances of getting sick.

Some medications that decrease the immune system include azathioprine, basiliximab, cyclosporine, daclizumab, muromonab-CD3, mycophenolate, tacrolimus, sirolimus, prednisone, corticosteroids (glucocorticoids), and others.

4.6 Use in special populations

Pregnancy

We found no evidence that taking probiotics or prebiotics during pregnancy either increases or decreases the risk of preterm birth or other infant and maternal adverse pregnancy outcomes. However, Vizylac GG drops are meant to be taken in children below 5 years of age.

Breast-feeding

Because probiotics are rarely systemically absorbed, they are not expected to transfer into breast milk. One randomized control trial examined *Lactobacillus reuteri* levels in 174 colostrum samples after maternal and infant oral supplementation of this probiotic. Although higher in the active than in the placebo group, the prevalence of *L reuteri* in colostrum was low and not clinically important. Abrahamsson et al suggested that the most likely origin of *L reuteri* in colostrum was external contamination from the gastrointestinal tract. There are no published data regarding adverse effects in breastfed infants. In several of the studies previously mentioned, infants received probiotic therapy after delivery without an increase in adverse effects.

Fertility

Results indicated that *Lactobacillus* intermitted colonization of pathogenic strains that resulted in reinforcement of natural microflora and resurge fertility.

4.7 Effects on ability to drive and use machines

Although there is no evidence of *lactobacillus* on ability to drive and use machine. Probiotics have ability to decrease metabolic endotoxemia by restoring the disrupted intestinal mucosal barrier.

4.8 Undesirable effects

Probiotics are generally regarded as safe, and side effects in ambulatory care have rarely been reported. Bacterial translocation, sepsis, and the risk of carrying antibiotic resistance plasmids that may spread resistance to antibiotics have been reported. The latter has been reported for some probiotics, such as *L. reuteri* ATCC 55730 and *Enterococcus faecium* but not for LGG.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this Medicine.

4.9 Overdose

If patient may has overdosed, may suffer from serious symptoms such as passing out or trouble breathing.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

The underlying mechanisms of probiotic action are unclear but may include strengthening of the non-immunological gut barrier, pathogen growth inhibition and interference with adhesion, and enhancement of mucosal immune systems, as well as the systemic immune

response. Probiotics appear effective in preventing and reducing the severity of a number of conditions, but there is insufficient evidence with respect to any suggested benefits from probiotics in prevention or therapy of ischemic heart diseases, autoimmune disease or cancer.

5.2 Pharmacodynamic properties

There are various proposed mechanisms by which probiotic may protect the host from intestinal disorders. Probiotics have an antimicrobial effect through modifying micro flora, secreting antibacterial substances, competing with pathogens to prevent their adhesion, competing with nutrients necessary for pathogen survival, producing an antitoxin effect and reversing some of the consequences of infection on the gut epithelium – such as secretory changes and neutrophil migration. Inhibitory substances such as organic acids, hydrogen peroxide and bacteriocins inhibits bacterial metabolism or toxin produced by bacteria. They also block the receptor sites by competitive inhibition for bacterial adhesion sites on intestinal epithelial surfaces. In addition to that, probiotics also competes with pathogenic microorganisms for the nutrition. In *C. difficile* intestinal disease, *S. boulardii* protects through degradation of the toxin receptor on the intestinal mucosa. Other proposed mechanisms include strengthening tight junctions between enterocytes, increasing IG-A. Production and stimulation of specific and nonspecific immunity. In sum, Probiotics are generally thought to affect the gastrointestinal tract and the associated CD (local) immune system. Several studies have been performed to investigate the effects of different probiotic bacteria. From these studies it has become clear that different strains of lactobacilli induce very different effects. In addition, effects seen in a certain human population with one strain of bacteria can often not be reproduced. This makes a final overall conclusion very difficult. Probiotic treatment is not known. The quality control of the commercialised probiotic food supplements, the exactness of the label and the indications need to be improved. More research on pharmacodynamic and pharmacokinetic aspects is also needed. Safety should be better assessed in pre-term, immunodeficient and immunocompetent individuals for any risk of overstimulation (or modification) of the immune system in susceptible subjects. The establishment of standards of identity for probiotic-containing food products will serve to accelerate their development and availability.

5.3 Pharmacokinetic properties

It has been shown that some probiotic strains can adhere to cell lines such as $CaCO_2$ or HT_{29}. These epithelial cell lines are of colonic or intestinal origin. The cells are polarized like in an intestinal epithelium, and many characteristics and functions of a normal epithelium are expressed on the cells. They are therefore thought to be fair models to predict in vivo adhesion. Using other cell lines or colon tissues have also been proposed. The epithelial adhesion property differs between strains, and this property might be correlated with competitive exclusion properties and immunomodulatory activities in vivo. Until now, competitive exclusion properties of adhering strains have only been shown in vitro. Validation of the in vitro models with in vivo data is therefore warranted, and the possibility for a probiotic to adhere to the intestinal epithelium during its intestinal transit has to be studied.

<u>Survival of ingested probiotics to different sites of the gastrointestinal tract</u>

The survival of ingested microorganisms differs among genus and strains. Some microorganisms are destroyed in the stomach while others have a high survival till feces. *Lactobacillus bulgaricus* and *Streptococcus thermophilus* have a poor intrinsic resistance to acid, and are destroyed within few minutes at pH 1 and in about 1 hr at pH 3. Using an intestinal intubation technique, we showed that one fifth of the lactase contained in yogurt bacteria survives till the end of the small bowel and participates to the digestion of lactose in the human

gut. It is to note that this effect does not need the bacteria to be of human origin, and does not require that they survive in the GIT (but even rather that they lyse there, releasing then the lactase that they contain). As the survival of yogurt bacteria is low in the upper gastrointestinal tract, their survival and probiotic effects downstream (in the colon) are probably not relevant. The capacities of survival of *L. acidophilus, L. reuteri, L. rhamnosus* strain GG in acid conditions are higher than that of *L. bulgaricus*. About 1-10% of *L. acidophilus* ingested in fermented products were found to survive until the ileum in several human studies using intestinal intubation techniques. In one of reported study, the concentrations of lactobacilli flowing through the ileum after ingestion of a cup of milk product containing 108 cfu/ml of Yoplait-Al strain were 100 times higher than the concentrations after ingestion of a control meal; the passage lasted for more than 5 hr, and no permanent colonization of the small bowel was observed. Studies in healthy volunteers ingesting different probiotic preparations showed that concentrations of *L. acidophilus, L. reuteri, L. rhamnosus* strain GG reached around 106 cfu/. Probiotics are usually excreted within a few days after their ingestion in feces at the same rate or even quicker than a transit marker.

6. Nonclinical properties

Safety assessment

These include pathogenicity, infectivity and virulence factors comprising toxicity, metabolic activity and intrinsic properties of the microbes. The classic risk assessment approach like that used for pathogens could be misleading for probiotic microbes. Factors such as adhesion which may lead to colonization are regarded as virulent factors in studies of pathogens. In contrast, most probiotic Lactobacilli strains are initially selected on the basis of their ability to adhere to the various mucosa models. However, some lactobacilli may produce biogenic amines such as tyramine and histamine, but no such potentially harmful compounds have been found in fermented milk prepared with probiotic lactobacilli. Some strains of probiotic lactobacilli are known to produce bacteriocins that are toxic to other pathogenic bacteria, but such molecules are nontoxic to humans and truly meet the requirements for food preservatives.

Toxicity-Related Assessment

Conventional toxicology and safety evaluation that is usually employed for pharmaceutical products may be of limited value in assessing the safety of probiotics. Toxicity testing has grown to maturity and presently a systematic approach is used to establish whether adverse effects occur and if so to investigate at level of exposure such adverse effects remain absent and whether a dose-response relationship can be established. On the basis of these findings, a safety evaluation may be performed to assess at what levels of exposure humans may not experience any risk. The safe levels of exposure for humans has been identified for individual chemicals in the risk assessment of compounds with known toxicological profiles. Attempt to develop safe level of exposure' to probiotic microbes may be complicated in that the microbial cell and human cell ratio is already 9:1. The Threshold of Toxicological Concern (TTC) will refers to the establishment of a level of exposure for existing probiotic microbes.

7. Description

Lactobacillus rhamnosus GG Drops is pale yellow coloured oil suspension filled in an amber coloured bottle.

The excipients used are medium chain triglyceride oil, Anticaking agent (INS 551), Antioxidant (INS 307).

8. Pharmaceutical particulars

8.1. Incompatibilities

Not available

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

VIZYLAC GG DROPS is packed in amber bottle.

8.4. Storage and handing instructions

Store below 25°C, protected from moisture and direct sunlight

9. Patient Counselling Information

Vizylac GG Drops

***Lactobacillus rhamnosus* GG Drops (ATCC 53103)**

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet?

9.1 What Vizylac GG Drops are and what they are used for.

Vizylac GG Drops contains active ingredient *Lactobacillus rhamnosus* and it is indicated as a probiotic food and for the restoration of microbial flora.

9.2 What you need to know before you use Vizylac GG Drops

Do not use Vizylac GG Drops

If you are allergic to *Lactobacillus rhamnosus* or to any of the other ingredients of this medicine.

Warning and Precautions

- Talk to your doctor or pharmacist before taking Vizylac GG Drops if you allergic to it; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to pharmacist for more details.
- If you have any of the following health problems, consult the doctor or pharmacist before using this product: diarrhea lasting more than 2 days (especially if you also have a high fever), weakened immune system (such as due to chemotherapy, HIV infection), recurring vaginal infections, recurring urinary tract infections.

Taking other medicines

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Vizylac GG Drops and certain other medicines can affect each other. Sometimes the dose of some of your other medicines or Vizylac GG Drops will have to be adjusted.

Antibiotic drugs interact with *LACTOBACILLUS*

Taking antibiotics along with *lactobacillus* can reduce the effectiveness of *lactobacillus*. To avoid this interaction, take lactobacillus products at least 2 hours before or after antibiotics.

Medications that decrease the immune system (Immunosuppressants) interacts with *LACTOBACILLUS*

Medications that decrease the immune system can increase your chances of getting sick from bacteria and yeast. Taking lactobacillus along with medications that decrease the immune system might increase the chances of getting sick.

Some medications that decrease the immune system include azathioprine, basiliximab, cyclosporine, daclizumab, muromonab-CD3, mycophenolate, tacrolimus, sirolimus, prednisone, corticosteroids (glucocorticoids), and others.

Vizylac GG Drops with food and drink

7 drops of Vizylac GG Drops should be taken per day before or after the first meal or as directed by healthcare professionals.

Pregnancy and breast-feeding

We found no evidence that taking probiotics or prebiotics during pregnancy either increases or decreases the risk of preterm birth or other infant and maternal adverse pregnancy outcomes and because probiotics are rarely systemically absorbed, they are not expected to transfer into breast milk while for fertility results indicated that *Lactobacillus* intermitted colonization of pathogenic strains that resulted in reinforcement of natural microflora and resurge fertility.

Driving and using machines

Vizylac GG Drops is not expected to affect the ability to drive or use machines.

9.3 How to use Vizylac GG Drops

Always take this medicine exactly as your doctor, pharmacist or nurse have told you. Check with your doctor, pharmacist or nurse if you are not sure. Vizylac GG Drops should be taken orally

Direction for use: Shake the bottle well until the suspended materials are dispersed. Remove the cap. Tilt the bottle at about 45° angle to release 7 drops in a spoon. Do not administer directly from the bottle into the mouth or add hot milk or food.

- To be given only under medical advice by physician/ certified dietician/ nutritionist for children below 5 years.
- 7 drops per day before or after the first meal or as directed by healthcare professionals.
- Use within 14 days from the date of opening under recommended storage condition; discard the unused material after 16 days. Keep the bottle closed.

How much will be given

7 drops per day before or after the first meal or as directed by healthcare professionals.

If you take more than you should

If you take too many drops, contact your nearest hospital casualty department or doctor immediately. Take this leaflet and any remaining drops with you to show the doctor.

Signs of a very bad reaction to the drug. These include wheezing; chest tightness; fever; itching; bad cough; blue or gray skin color; seizures; or swelling of face, lips, tongue, or throat. Any rash. Side effect or health problem is not better or you are feeling worse.

If you forget to take Vizylac GG Drops.
If you forget to take your drops, take them as soon as you remember and then continue with the next dose as instructed. Do not take a double dose to make up for a forgotten dose.

If you stop taking Vizylac GG Drops
To get the most benefit from Vizylac GG Drops, always finish the course of treatment recommended by your doctor or pharmacist. If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

9.4. Possible side effects

Probiotics are generally regarded as safe, and side effects in ambulatory care have rarely been reported. Bacterial translocation, sepsis, and the risk of carrying antibiotic resistance plasmids that may spread resistance to antibiotics have been reported. The latter has been reported for some probiotics, such as *L. reuteri* ATCC 55730 and *Enterococcus faecium* but not for LGG.

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By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store Vizylac GG Drops

Store below 25°C, protected from moisture and direct sunlight.

9.6 Contents of the pack and other information

Each dosage (7 drops/0.25ml) contains:

Lactobacillus rhamnosus GG Drops……1 Billion CFU
(ATCC 53103)

Ingredients: Medium chain triglyceride oil, *Lactobacillus rhamnosus* GG Drops (ATCC 53103), Anticaking agent (INS 551), Antioxidant (INS 307).

No added flavours or colours.

VIZYLAC GG DROPS is packed in amber bottle.

10. Details of manufacturer

Under collaboration with:
Blumen Biovitals Healthcare Pvt. Ltd.
Manufactured by:
Sunberg Lifesciences Pvt. Ltd.
No. C-75, 76, 77,15th Cross, PIPDIC Industrial Estate, Mettupalayam, Puducherry-605009, India.

11. Details of permission or licence number with date

FSSAI Lic No. 10019045000159 issued on 31.12.2020

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ VIZYLAC GG DROPS- 1.0 Billion CFU /JUL-21/01/PI