40427 P4

BIOGEN
FOR THE RESULTS YOU WANT

RE | NU DEBLOAT & DIGEST

PROFESSIONAL INFORMATION

D 33.6 Western Herbal Medicine. Complementary medicine.

This unregistered medicine has not been evaluated by SAHPRA for its quality, safety or intended use. Health supplements are intended only to complement health or supplement the diet.

SCHEDULING STATUS: S0

1. NAME OF THE MEDICINE
BIOGEN RE | NU DEBLOAT & DIGEST

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vegetarian capsule contains:		%NRV*
Silybum marianum (Milk thistle) [Seed, extract standardised to 80 % silymarin providing 160,00 mg Silymarin]	200,00 mg	
Aloe ferox bitter powder (Aloe vera) [Leaf, standardised to 8-14 % Hydroxyanthracene derivatives, as anhydrous barbaloin]	150,00 mg	
DigeZyme® (multi-enzyme blend) Containing:	150,00 mg	
α-Amylase (as *Aspergillus oryzae*)	3 600 FCC DU	
Protease (as *Bacillus subtilis*)	900 FCC PC	
Lactase (as *Aspergillus oryzae*)	600 FCC ALU	
Lipase (as *Rhizopus oryzae*)	150 FCC FIP	
Cellulase (as *Trichoderma longibrachiatum*)	30 FCC CU	
Afriplex® GRT (*Aspalathus linearis* (Burn.f.) R. Dahlgren (Green Rooibos)) [Leaves, 5:1 extract providing 500,00 mg dried herb equivalent]	100,00 mg	
Curcuma longa L. (Turmeric) [Root; Extract standardised to 95 % curcumins]	80,00 mg	
Riboflavin (Vitamin B_2)	50,00 mg	3 846 %
Melissa officinalis L. (Lemon balm) [Leaf; 10:1 Extract providing 135,00 mg dried herb equivalent]	13,50 mg	

*%Nutrient Reference Values (NRVs) for individuals 4 years and older (2010)

Sugar free

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Vegetable Capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RE | NU DEBLOAT & DIGEST, supports abdominal comfort, optimal digestion and promote bowel movement for relief from occasional constipation, and digestive upset.

4.2 Posology and method of administration

Adults: Take 1 (one) capsule daily with meals, if required or as recommended by your healthcare provider. Allow at least 6-12 hours for laxative effect to occur.

The safety and efficacy of RE | NU DEBLOAT & DIGEST in children has not yet been established. Not allowed in children under 18 years.

4.3 Contraindications

- If you have a hypersensitivity to Milk thistle, Aloe ferox, DigeZyme®, Green rooibos, Turmeric, Vitamin B_2 and Lemon balm or any of the excipients listed in 6.1.
- Not recommended for patients with abnormal constrictions of the gastrointestinal tract, potential or existing intestinal blockage, atonic bowel, appendicitis, inflammatory colon disease (e.g. Crohn's disease or ulcerative colitis), abdominal pain of unknown origin, undiagnosed rectal bleeding, severe dehydration with depleted water or electrolytes, hemorrhoids or diarrhea.
- Not recommended during pregnancy and lactation.

4.4 Special warnings and precautions for use

Special care should be taken with RE | NU DEBLOAT & DIGEST

If you are taking any prescribed medication, please check with your healthcare provider before taking this medicine. Please take note of the following:

- Consult a healthcare provider if symptoms persist or worsen.
- Consult a healthcare provider prior to use if you have faecal impaction or symptoms such as abdominal pain, nausea, vomiting or fever.
- Consult a relevant health care provider before use if you have malabsorption or other GIT ailments or are having surgery; or are taking blood thinners, antibiotics or anti-inflammatory medication.
- Consult a healthcare provider prior to use if you have a kidney disorder, or are taking cardiac medications (e.g. cardiac glycosides or antiarrhythmic medications).
- Consult a healthcare provider prior to use if you are taking thiazide diuretics, corticosteroids, licorice root, or other medications or health products that may aggravate electrolyte imbalance.
- Reduce dose or stop use if you experience abdominal pain, cramps, spasms and/or diarrhea.
- Consult a relevant health care provider before use if you are pregnant or breastfeeding, or for use beyond four (4) weeks.
- RE | NU DEBLOAT & DIGEST is not recommended for use in children under the age of 18 years.
- Consumers should discontinue use and consult a relevant health care provider if they experience symptoms of low blood sugar such as sweating, paleness, chills, headache, dizziness and/or confusion.

Nutritional supplementation should not replace a balanced diet. Do not exceed the recommended dose without consulting a healthcare provider.

4.5 Interaction with other medicines and other forms of interaction

Interactions with Medicines

- Milk thistle and Aloe can lower blood glucose levels and glycated hemoglobin (HbA1c) in patients with type 2 diabetes, including those already taking antidiabetes drugs, caution is advised when taking Milk thistle with antidiabetic drugs.
- Milk thistle should be used cautiously in patients receiving estrogen therapy.
- Use caution when taking milk thistle in combination with medicines metabolized by the cytochrome P450 2C9 (CYP2C9) enzyme. These medicines include amitriptyline, diazepam, verapamil, warfarin and zileuton.
- Use caution when taking milk thistle in combination with medicines metabolized by the cytochrome P450 2D6 (CYP2D6) enzyme. These medicines include tricyclic antidepressants such as imipramine and amitriptyline, antipsychotics such as haloperidol, risperidone and chlorpromazine; beta-blockers such as propranolol, metoprolol, carvedilol and tamoxifen.
- Use caution when taking milk thistle in combination with medicines metabolized by the cytochrome P450 3A4 (CYP3A4) enzyme. These medicines include alprazolam, amlodipine, clarithromycin, cyclosporine, erythromycin, lovastatin, ketoconazole, itraconazole, fexofenadine, triazolam and verapamil.
- Milk thistle may decrease the clearance of sirolimus in hepatically impaired renal transplant patients. Use milk thistle cautiously in combination with sirolimus.
- Use milk thistle with caution when taking other medications that could undergo glucuronidation. These medicines include acetaminophen, oxazepam, haloperidol, lamotrigine, morphine, zidovudine as well as raloxifene. Tamoxifen; Indinavir; Statins.
- Aloe might increase the risk of bleeding when taken with anticoagulant or antiplatelet drugs.
- Aloe can increase the risk of adverse effects from cardiac glycoside drugs, such as digoxin, due to potassium depletion, caution is advised.
- Aloe might increase the risk of hypokalemia when taken with diuretic drugs and might increase the risk for fluid and electrolyte loss when taken with stimulant laxatives.
- Caution is advised with concomitant use of Aloe and Warfarin as it might increase the risk of bleeding.
- Concomitant use of blood pressure lowering medication such as angiotensin-converting enzyme (ACE) inhibitors, antihypertensive herbs/supplements or calcium channel blockers, as rooibos, may have additive blood pressure lowering effects.
- Theoretically, combining rooibos and atorvastatin could increase the effects and side effects of atorvastatin, whereas vitamin D oppositely may reduce the absorption of atorvastatin.
- Vitamin B_2 (Riboflavin): Large doses result in a bright yellow discoloration of the urine that may interfere with certain laboratory tests.
- Vitamin B_2 may theoretically decrease the effectiveness of broad-spectrum antibiotics (quinolones or tetracyclines).
- Concomitant use of lemon balm might have additive effects with CNS depressant drugs and caution is advised in patients taking CNS depressant drugs.

Interactions with Diseases/Impairments

- Milk thistle may cause an allergic reaction in individuals sensitive to the Asteraceae/Compositae family. Members of this family include ragweed, chrysanthemums, marigolds, daisies, and many other herbs.
- Patients with hormone sensitive conditions should avoid using milk thistle due to its estrogenic effects. Some of these conditions include breast cancer, uterine cancer, ovarian cancer, endometriosis, and uterine fibroids. Silymarin, a milk thistle constituent, can bind to estrogen receptor beta.
- Due to the irritating effects of its anthranoid aloin constituents, aloe is contraindicated in individuals with intestinal obstruction, acute intestinal inflammation (Crohn disease, ulcerative colitis, appendicitis), ulcers, abdominal pain of unknown origin, nausea, and vomiting.
- Taking aloe orally might exacerbate kidney disorders. High doses of aloe have been linked to nephritis and kidney failure.
- Patients with liver disease, such as hepatitis, biliary obstruction, cirrhosis etc., may experience manganese accumulation and toxicity and decreased vitamin B_2 absorption. Theoretically, chromium might exacerbate liver disease. Vitamin B_2 absorption is decreased in patients with liver disease such as hepatitis, biliary obstruction, and cirrhosis.
- Lemon balm may alter thyroid function, reduce thyroid hormone levels, and interfere with thyroid hormone replacement therapy. In vitro, constituents of lemon balm extract bind to thyroid stimulating hormone (TSH), preventing TSH receptor binding and leading to the inhibition of TSH-stimulated adenylate cyclase activity.

Interactions with Foods

- Vitamins, minerals and nutrients obtained from other sources should be taken into account when prescribing/ suggesting RE | NU DEBLOAT & DIGEST.
- Alcohol may increase the risk of sedation, caution is advised.
- Alcohol intake for longer than 2 weeks may impair the absorption of Vitamin B_{12}.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established and is contraindicated in pregnancy (see section 4.3).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machinery have been performed. It is advised that patients taking RE | NU DEBLOAT & DIGEST should not drive or operate machinery until they are reasonably certain that it does not adversely affect their ability to drive or operate machinery.

4.8 Undesirable effects

Orally, Milk thistle, Aloe ferox, DigeZyme®, Green rooibos, Turmeric, Vitamin B_2 and Lemon balm is well-tolerated.

Summary of adverse reactions

Gastrointestinal disorders:

Frequent: Milk thistle can cause mild gastrointestinal symptoms have been reported, including nausea, vomiting, bloating, diarrhea, epigastric pain, abdominal colic or discomfort, dyspepsia, dysgeusia, flatulence, constipation, and loss of appetite. Aloe may cause abdominal pain, cramps, and diarrhea. Turmeric may cause constipation, dyspepsia, diarrhea, distension, gastroesophageal reflux, nausea, and vomiting.

Frequency unknown: Dry mouth, and flu-like symptoms.

Musculoskeletal:
Frequency unknown: Breast soreness.

Dermatologic:
Frequency unknown: Milk thistle may cause urticaria, eczema, skin rash, and anaphylaxis. Skin irritation, skin rash pruritus, and urticaria.

Other:
Frequency unknown:
Large/long term dosages might cause hepatotoxicity in some patients.
Orally, turmeric has been associated with liver damage, including non-infectious hepatitis, cholestasis, and hepatocellular liver injury.
Orally, the turmeric constituent curcumin can cause vertigo, but this effect seems to be uncommon.

Description of selected adverse reactions
RE | NU DEBLOAT & DIGEST with Milk thistle, Aloe ferox, DigeZyme®, Green rooibos, Turmeric, Vitamin B_2 and Lemon balm may cause several adverse reactions, including nausea, vomiting, bloating, diarrhea, epigastric pain, abdominal colic or discomfort, dyspepsia, dysgeusia, flatulence, constipation, and loss of appetite. Aloe may cause abdominal pain, cramps, and diarrhea.

Paediatric Population
RE | NU DEBLOAT & DIGEST is not recommended for use in children under the age of 18 years.

Other special populations
No clinical data are available on the effects of RE | NU DEBLOAT & DIGEST on other special populations.

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 via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: *http://www.sahpra.org.za/Publications/Index/8.*

4.9 Overdose

Side effects listed in section 4.8 can be precipitated and/or be of increased severity.

In the event of overdose, treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Mechanism of action:

Milk thistle, contains active constituent, silymarin, and is most often used for liver disorders, including liver damage caused by chemicals, alcohol, and chemotherapy, as well as liver damage cause by Amanita mushroom poisoning, non-alcoholic fatty liver disease, chronic inflammatory liver disease, cirrhosis of the liver, and chronic hepatitis. Silymarin possesses antioxidant properties and reduces inflammatory cytokines.

Aloe ferox, used for inflammatory bowel diseases and ulcers. Anthraquinones contain a tricyclic anthracene nucleus and are cleaved to form anthrones in the colon which are responsible for potent laxative effects.

DigeZyme®, a unique, proprietary blend of five specific enzymes, viz. α-amylase (starch digestive enzyme), protease (protein digestive enzyme), lipase (Fat digestive enzyme), cellulose (cellulose hydrolyzing enzyme), and lactase (lactose hydrolyzing enzyme). This provides optimal digestion of all the macromolecules.

Green rooibos, unknown.

Turmeric, turmeric or its constituents increased bowel motility.

Vitamin B_2, Converted to the co-factors, flavin mononucleotide (FMN) and flavin-adenine dinucleotide (FAD), in the body. These cofactors attach and consequently activates flavoproteins. Flavoproteins play a role in many enzymatic and metabolic processes in the body.

Lemon balm, is known to be a potent in vitro inhibitor of rat brain GABA transaminase and monoamine oxidase A (MAO-A).

Pharmacodynamic effects:

Milk thistle, used as a liver protectant and to support the liver function.

Aloe ferox, the exudate of Aloe ferox contains 15-40 % anthrone 10-C-glucosides (anthraquinone derivatives) such as hydroxyaloins and aloin. Aloin is a mixture of the stereoisomers aloin a (barbaloin) and aloin B (isobarbaloin). Furthermore, the exudate contains the pyrone derivative aloenin and free and glucosylated 2-acetonyl-7-hydroxy-5-methylchromones. (e.g., aloesone, furoaloesone, Aloe resin A, Aloe resin B (aloesin) and aloeresin C). Aloe ferox also contains glycosylated feroxidin (a tetralin) and feralolide (a dihydroisocoumarin). Aloin is an inactive laxative compound, it becomes an active aloe emodin anthrone by Eubacterium sp. and responsible for laxative properties..

DigeZyme®, the gastrointestinal tract begins with the mouth, and digestion starts with chewing, which breaks up large pieces of food into smaller particles that can be swallowed. The saliva contains the digestive enzyme amylase, which breaks complex sugars, into smaller sugar units. The food is then moved to the stomach where it is subjected to enzymatic action enteric digestive enzymes viz., protein-digesting enzyme (pepsin), and lipid digesting enzyme (gastric lipase). The final stage of digestion and most of the absorption occurs in the small intestine. Here, partially digested carbohydrates, fats, and proteins are broken down by respective digestive enzymes into monosaccharides, fatty acids, and amino acids, respectively.

Green rooibos, has antioxidant properties which may reduce the risk of type 2 diabetes (T2DM) and its complications.

Turmeric, curcumin improved activity of digestive enzymes. In animal research, turmeric and its constituent curcumin reduced the incidence of gastrointestinal ulcers and increased intestinal wall mucus and non-protein sulfhydryl content. Evidence from animal models also suggests that turmeric and its constituent curcumin reduce injury related to inflammatory colitis.

Vitamin B_2, Water-soluble B vitamin involved in vital metabolic processes and is necessary for normal cell growth, function, and energy production.

Lemon balm, has sedative, spasmolytic, and antibacterial effects. Lemon balm contains the flavonoids, monoterpenoid and sesquiterpenes.

Pharmacokinetic properties

Absorption:

Milk thistle, Bioavailability data for milk thistle in humans are controversial because of the complexity of the composition and the diversity of the constituents. After oral doses of 140-560 mg, silybin A accounted for 84% of measurable flavonolignans in plasma.

Aloe ferox, There is insufficient reliable information available about the pharmacokinetics of aloe.

DigeZyme®, unknown.

Green rooibos, unknown.

Turmeric, bioavailability of curcumin is very low. The average peak serum concentrations after taking curcumin 4 grams, 6 grams, and 8 grams were 0.51 mcM, 0.63 mcM, and 1.77 mcM, respectively.

Vitamin B_2, Absorbed from the gastrointestinal tract. Absorption mechanism for riboflavin is saturable.

Lemon balm, peak concentration of rosmarinic acid at 30 min to 1 hour post ingestion, before returning to baseline levels.

Distribution/Metabolism/Excretion:

No clinical data are available on the effects of RE | NU DEBLOAT & DIGEST

Milk thistle,
Metabolism: Silymarin flavonolignans undergo rapid first-pass conjugation.
Excretion: Silymarin flavonolignans undergo biliary excretion. After oral intake, less than 10 % of silymarin is excreted in the urine, and 20 % to 40 % is recovered in the bile as glucuronide and sulfate conjugates. The elimination half-lives for milk thistle constituents are generally less than 4 hours, with most ranging between 0.8-2.4 hours.

Aloe ferox, There is insufficient reliable information available about the pharmacokinetics of aloe.

DigeZyme®, unknown.

Green rooibos, unknown.

Turmeric,
Metabolism: Curcumin undergoes significant metabolism in the liver and intestines, contributing to low oral bioavailability. In humans, curcumin is present in the plasma as glucuronide and sulfate conjugates. The half-lives of these conjugates are 6-24 hours.
Excretion: In humans, curcumin is present in the feces following consumption of an extract. In some studies, curcumin was undetectable in the urine following oral intake; however, other studies detected curcumin and its conjugates in the urine.

Vitamin B_2,
Distribution: Widely distributed to tissues; however, little is stored in the spleen, liver, heart, and kidneys.
Metabolism: Hepatically metabolized.
Excretion: Vitamin B_2 is excreted in the urine.

Lemon balm,
Distribution: Rapidly absorbed through the lungs and cross the blood-brain barrier.
Metabolism: Metabolized by gut microbiota. As rosmarinic acid (RA) is also metabolized to methyl-RA, caffeic acid and ferulic acid. RA and its metabolites are present in plasma and urine, predominantly as conjugated forms such as glucuronide or sulfate. Metabolism of RA may be altered by the presence of other factors such as dietary phenolics, food intake, disease states and drugs.
Excretion: Rapidly metabolised and excreted, approximately 50 % of the oral dose excreted within 24 hours. Eliminated through urine but most of the compound was excreted in feces, suggesting a role for the first-pass metabolism through the skin.

Preclinical safety data
When used orally and appropriately in adults, RE | NU DEBLOAT & DIGEST is recognized as possibly safe.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vegetable capsules, Magnesium stearate.

6.2 Incompatibilities

No compatibility studies has been performed, RE | NU DEBLOAT & DIGEST must not be mixed with other medications.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store in a cool, dry place at or below 25 °C.
Do not use after expiry date.
Keep the container tightly closed.
Protect from light.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

The container is a 175 ml PET container.
The cap is a silver plastic cap with a tamper evident seal.
Packed in a unit carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Biogen
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8. REGISTRATION NUMBER
Will be allocated by SAHPRA upon registration.

9. DATE OF FIRST AUTHORISATION
Will be allocated by SAHPRA upon registration.

10. DATE OF REVISION OF THE TEXT
This leaflet was last revised in June 2022.