39650 P3

BIOGEN
FOR THE RESULTS YOU WANT

MULTI VITAMIN DIABETIC

PROFESSIONAL INFORMATION

D 33.7 Combination Product. Complementary Medicine: Discipline-Specific
Health supplements are intended only to complement health or supplement the diet.

This unregistered medicine has not been evaluated by SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS: S0

1. NAME OF THE MEDICINE
BIOGEN MULTIVITAMIN DIABETIC (capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each BIOGEN MULTIVITAMIN DIABETIC capsule contains:

		%NRV*
Magnesium oxide (providing 150,00 mg elemental magnesium)	248,74 mg	36
Potassium chloride (providing 80,00 mg elemental potassium)	152,54 mg	
Zinc gluconate (providing 15,00 mg elemental zinc)	104,55 mg	136
Afriplex® GRT [*Aspalathus linearis* (Burn.f.) R. Dahlgren (Green Rooibos)] [Leaves, 5:1 extract providing 500,00 mg dried herb equivalent]	100,00 mg	
Ascorbic acid (Vitamin C)	50,00 mg	50
Iron amino acid chelate (providing 9,00 mg elemental iron)	45,00 mg	250
Manganese amino acid chelate (providing 2,00 mg elemental manganese)	20,00 mg	87
Nicotinamide (Vitamin B_3)	20,00 mg	125
α-Tocopheryl acetate (Vitamin E)	22,35 IU 15,00 mg α-TE	149
Pantothenic acid (Vitamin B_5) (from calcium D-pantothenate)	10,00 mg	200
Pyridoxine (Vitamin B_6) (from pyridoxine hydrochloride)	3,00 mg	176
Riboflavin (Vitamin B_2)	1,70 mg	131
Thiamine (Vitamin B_1) (from thiamine hydrochloride)	1,50 mg	125
Retinol (Vitamin A) (from retinyl acetate)	3 000,00 IU 900,09 µg RE	100
Chromium polynicotinate (providing 50,00 µg elemental chromium)	500,00 µg	143
Folic acid (Vitamin B_9)	400,00 µg	400
Cyanocobalamin (Vitamin B_{12})	40,00 µg	1 667
D-biotin (Vitamin B_7)	30,00 µg	100
Cholecalciferol (Vitamin D_3)	1 000,00 IU 25,00 µg	167

*%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
Capsules (30's).
White, size 00 gelatine capsules

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
BIOGEN MULTIVITAMIN DIABETIC, with chromium and Afriplex® GRT. A multivitamin and mineral supplement to replenish vitamins and minerals that are often deficient in diabetics.

4.2 Posology and method of administration
Adults and children over 12 years of age:
Posology
Adults: Take one (1) capsule daily with food, or as recommended by your healthcare practitioner. Not recommended for use in children.

Method of administration
Take BIOGEN MULTIVITAMIN DIABETIC capsules orally.

Special populations
Renal insufficiency increases the likelihood of toxicity due to hypermagnesemia or hyperkalemia.

Paediatric/Adolescent population
BIOGEN MULTIVITAMIN DIABETIC is not recommended for use in children or adolescents below 18 years of age.

4.3 Contraindications
- Hypersensitivity to chromium, iron, magnesium, manganese, potassium, rooibos, vitamin A, vitamin B_1, vitamin B_2, vitamin B_3, vitamin B_5, vitamin B_6, vitamin B_7, vitamin B_9, vitamin B_{12}, vitamin C, vitamin D_3, vitamin E, zinc, or other excipients listed under section 6.1.
- Patients with reduced kidney function - due to an increased risk of hypermagnesemia, hyperkalemia, and hyperoxaluria.
- Patients with iron-overloaded states such as hereditary hemochromatosis, hemosiderosis, or those who have a history of haemolytic anemia.

4.4 Special warnings and precautions for use
- Magnesium and vitamin E might theoretically increase the risk of bleeding – use with caution in patients with existing bleeding disorders.
- Use with caution in patients with renal disease, as BIOGEN MULTIVITAMIN DIABETIC may increase the risk for, or exacerbate kidney disease.
- Use with caution in patients with hepatic disease, as BIOGEN MULTIVITAMIN DIABETIC may increase the risk for, or exacerbate liver disease.
- Use vitamin C with caution in patients who are prone to oxalate stone formation.
- Vitamin D may increase the risk for hypercalcemia, kidney stones and calcified tissue in patients with sarcoidosis, lymphoma, hyperparathyroidism, histoplasmosis, tuberculosis, or those taking vitamin D supplementation .
- Iron overload is likely to occur in patients with hemoglobinopathies or other refractory anaemias incorrectly diagnosed as iron deficiency anaemia – use with caution.
- Iron supplementation is associated with an increased risk of nosebleed in patients with hereditary haemorrhagic telangiectasia (HHT) – use with caution.
- Patients with coronary stents should avoid vitamin B_6, vitamin B_9 and vitamin B_{12} supplementation, as it may increase the rate of restenosis.
- Patients receiving parenteral nutrition are at increased risk of manganese toxicity, which may result in a permanent neurological disorder.
- Use with caution in patients with a history of haemorrhagic stroke.
- Discontinue use at least 2 weeks prior to elective surgical procedures.
- Not recommended in women of childbearing age, those planning pregnancy, and those who are pregnant, or breastfeeding.
- Not to be given to children under the age of 18 years (see section 4.8 d).

4.5 Interaction with other medicines and other forms of interaction
Interactions with Medicines
Alkylating agents: Vitamin C and vitamin E may theoretically reduce the effectiveness of alkylating agents.
Antiarrhythmics: Vitamin B_6 may theoretically increase photosensitivity caused by amiodarone.
Antibiotics: Magnesium, iron, manganese, zinc and vitamin B_2 may theoretically decrease the effectiveness of broad-spectrum antibiotics (quinolones or tetracyclines). Zinc may decrease the absorption of cephalosporin antibiotics (cephalexin). Vitamin C and vitamin E may reduce the effectiveness of antitumor antibiotics. Magnesium may increase the risk for neuromuscular weakness when used concomitantly with bactericidal antibiotics, such as amikacin, gentamicin, streptomycin, tobramycin, and neomycin.
Anticoagulant/antiplatelet supplements/herbs: Magnesium and vitamin E may theoretically increase the risk of bleeding due to its antiplatelet properties – avoid using concomitantly with anticoagulants/antiplatelets.
Antihypertensives: Concomitant use of blood pressure lowering medication such as angiotensin-converting enzyme (ACE) inhibitors, antihypertensive herbs/supplements or calcium channel blockers, as rooibos, magnesium, and vitamin B_6 may have additive blood pressure lowering effects. Iron may affect methyldopa (antihypertensive) levels by reducing its absorption.
Antiparasitics: Vitamin B_9 may antagonize the antiparasitic effects of pyrimethamine against toxoplasmosis and Pneumocystis carinii pneumonia.
Antipsychotics: Concomitant use of manganese and antipsychotics, such as haloperidol, phenothiazine-derivatives, or others, may increase the risk of manganese toxicity. Vitamin C may theoretically decrease fluphenazine levels.
Barbiturates: Vitamin B_9 may have an antagonistic effect on primidone and phenobarbital, consequently increasing the risk for seizures.
Bisphosphonates: Magnesium and iron may decrease the absorption of bisphosphonates, thus affecting bone density loss.
Blood glucose lowering agents/herbs: Magnesium and chromium may theoretically result in additive blood glucose lowering.
Cardiac glycosides: Magnesium may decrease the therapeutic effect of cardiac glycosides, such as digoxin.
Central nervous system (CNS) agents: Magnesium, iron and vitamin B_6 may affect levodopa levels.
Chemotherapy medication: Zinc may theoretically inactivate cisplatin and its therapeutic effects. Vitamin B_9 may reduce the efficacy of methotrexate when using concomitantly.
Cytochrome substrates: Vitamin D and vitamin E may decrease the bioavailability of CYP3A4 substrates, by inducing CYP3A4 metabolism.
Heavy metal antagonists: Iron and zinc may affect penicillamine levels by reducing its absorption.
Hormones: Iron, chromium and vitamin C may affect the thyroid hormone, levothyroxine. Vitamin C may also increase plasma estrogen levels.
Immunosuppressants: Iron may affect mycophenolate mofetil (inhibitor for the prevention of transplant rejection) levels by reducing its absorption.
Integrase inhibitors: Iron and zincmay decrease integrase inhibitor (such as dolutegravir) levels and the effect of these medication.
Kinase inhibitors: Selumetinib contains vitamin E and may increase the risk of bleeding when using concomitantly with vitamin E supplements.
Metals: Vitamin C and vitamin D may increase aluminium absorption.
Minerals: Boron supplementation may decrease the excretion of magnesium in some people, and vitamin D may increase the absorption of calcium in the intestine.
Nonsteroidal anti-inflammatories: Nonsteroidal anti-inflammatories may increase chromium absorption and retention.
Potassium-sparing diuretics: The concomitant use of magnesium or potassium and potassium-sparing diuretics may respectively increase magnesium and potassium levels, resulting in hypermagnesemia or hyperkalaemia.
Protease inhibitors: When using regularly, zinc may prevent the absorption of atazanavir/ritonavir.
Retinoids: Concomitant use of vitamin A and retinoids may result in supratherapeutic vitamin A levels with additive toxic effects.
Statins: 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 D_3 derivatives: Concomitant use of calcipotriene with vitamin D may increase the risk for hypercalcemia.

Interactions with Diseases/Impairments
Achlorhydria: The absence of hydrochloric acid in gastric secretions causes decreased stomach acidity, and consequently impaired iron absorption.
Angioplasty: Patients with coronary stents should avoid vitamin B_6, vitamin B_9 and vitamin B_{12} supplementation, as it may increase the rate of restenosis.
Bleeding disorders: Magnesium and vitamin E might theoretically increase the risk of bleeding – use with caution in patients with existing bleeding disorders.
Cobalamin/cobalt hypersensitivity: Vitamin B_{12} contains cobalamin and cobalt, and may cause allergic reactions in patients who are sensitive to both these compounds.
Fat malabsorption disorders: Patients with fat absorption diseases such as short gut syndrome, celiac disease, obstructive jaundice, cystic fibrosis, pancreatic disease, and cirrhosis of the liver, may experience reduced vitamin A absorption.
Haemodialysis: Iron, and vitamin B_1 absorption is decreased in patients receiving haemodialysis. Haemodialysis might also increase vitamin B_7 excretion.
Haemoglobin diseases: Iron overload is likely to occur in patients with hemoglobinopathies or other refractory anemias incorrectly diagnosed as iron deficiency anemia.
Hereditary haemorrhagic telangiectasia (HHT): Iron supplementation is associated with an increased risk of nosebleed in patients with HTT.
Histoplasmosis: Vitamin D may increase calcium levels in patients with histoplasmosis. This is due to the increased metabolism of vitamin D to calcitriol, increasing the risk for hypercalcemia, kidney stones and calcified tissue – use with caution.
Hyperparathyroidism: Vitamin D may increase calcium levels and lead to hypercalcemia in people with hyperparathyroidism.
Kidney stones: Vitamin C may increase the risk of oxalate kidney stones, especially in patients who are prone to oxalate stone formation.
Liver disease: 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.
Lymphoma: Vitamin D may increase calcium levels in people with lymphoma, consequently increasing the risk for hypercalcemia, kidney stones and calcified tissue – use vitamin D supplements with caution.
Renal disease: Due to an increased risk of hypermagnesemia, hyperkalemia, or hyperoxaluria - use with caution in patients with reduced kidney function. Theoretically, chromium might exacerbate kidney disease. Vitamin D may increase calcium levels and increase the risk of arteriosclerosis in patients with renal failure.
Sarcoidosis: Vitamin D may increase calcium levels in people with sarcoidosis, consequently increasing the risk for hypercalcemia, kidney stones and calcified tissue – use vitamin D supplements with caution.
Stroke: Vitamin E might theoretically increase the risk of haemorrhagic stroke – use with caution in patients with a history of haemorrhagic stroke.
Surgical procedures: Vitamin E might increase the risk of bleeding if used perioperatively - Discontinue use at least 2 weeks prior to elective surgical procedures.
Tuberculosis: Vitamin D may increase calcium levels in patients with tuberculosis, consequently increasing the risk for hypercalcemia, kidney stones and calcified tissue – use vitamin D supplements with caution (see section 4.4).
Interactions with Foods
Alcohol: Alcohol decreases the conservation of magnesium via the kidneys, thus increasing the risk for magnesium deficiency. Long-term/excessive alcohol consumption is associated with impaired zinc absorption and increased excretion of zinc in the urine. Chronic alcohol ingestion may exacerbate the effects of vitamin A, particularly hepatotoxicity. Chronic alcohol abusers may experience an increase in urinary vitamin C excretion.
Smoking: Smoking theoretically increases vitamin B_7 catabolism which might cause minor vitamin B_7 deficiency.

4.6 Fertility, pregnancy and lactation
Adults (18 years and older)
Chromium - likely safe when used orally and appropriately during pregnancy at a dosage of 30 µg daily, and during lactation at a dosage of 45 µg daily.
Iron - likely safe when used at a dosage below 45 mg elemental Iron daily in pregnant and breastfeeding patients with adequate iron stores.
Magnesium - likely safe when used orally and appropriately at a dosage of 350 mg daily in pregnant and breastfeeding women.
Manganese - likely safe for pregnant and lactating women when used orally and appropriately at a dosage below 11 mg daily.
Potassium - likely safe for pregnant and lactating women when used at a dosage of 40-80 mEq daily.
Rooibos - Insufficient reliable information available.
Vitamin A - likely safe during pregnancy and lactation when used in doses less than 3 000 µg per day.
Vitamin B_1 - Safety of supplemental Vitamin B_1 is unknown.
Vitamin B_2 - Safety of supplemental Vitamin B_2 is unknown.
Vitamin B_3 - Safety of supplemental Vitamin B_2 is unknown.
Vitamin B_5 - likely safe when used orally and appropriately during pregnancy and lactation. The adequate daily intake during pregnancy is 6 mg, and 7 mg daily during lactation.
Vitamin B_6 - likely safe when used orally and appropriately at a dosage of 75 mg daily during pregnancy, and 2 mg during lactation.
Vitamin B_7 - likely safe when used orally and appropriately at a dosage of 30 µg daily during pregnancy, and 35 µg daily during lactation.
Vitamin B_9 - likely safe when used orally and appropriately during pregnancy and lactation at a dosage of 1 000 µg daily.
Vitamin B_{12} - likely safe when used orally and appropriately at a dosage of 2,6 µg daily during pregnancy, and 2,8 µg during lactation.
Vitamin C - likely safe when used orally and appropriately in pregnant and breastfeeding women at a dosage of 2 000 mg daily.
Vitamin D_3 - likely safe when used orally and appropriately in pregnant and breastfeeding women at a dosage of 100 µg daily.
Vitamin E - possibly safe when used orally and appropriately in pregnant and lactating women at a dosage not exceeding 1 000 mg daily.
Zinc - likely safe when used orally and appropriately in pregnant and breastfeeding women at a dosage of 40 mg daily.

4.7 Effects on ability to drive and use machines
BIOGEN MULTIVITAMIN DIABETIC may affect the ability to drive or operate machinery, as it may cause headache and somnolence.
Please exercise care until you are certain that your ability to perform such activities is not affected.

4.8 Undesirable effects
4.8 a Summary of safety profile
When used orally and appropriately, chromium, iron, magnesium, manganese, potassium, vitamin A, vitamin B_1, vitamin B_{12}, vitamin B_2, vitamin B_5, vitamin B_6, vitamin B_7, vitamin B_9, vitamin C, vitamin D, vitamin E, and zinc is generally well tolerated when using as prescribed. Insufficient reliable information available about the safety of rooibos and vitamin B_3 when used orally in medicinal amounts.

4.8 b Summary of adverse reactions
Gastrointestinal disorders (Frequent): Abdominal pain, esophagitis, heartburn, constipation, belching, flatulence, gastrointestinal irritation, diarrhoea, nausea, metallic taste in mouth, and vomiting.
Gastrointestinal disorders (Frequency unknown): Dry mouth, and flu-like symptoms.
Dermatological disorders (Frequency unknown): Skin irritation, skin rash pruritus, and urticaria.
Neurological disorders (Frequency unknown): Headache and somnolence.
Musculoskeletal disorders (Frequency unknown): Breast soreness.

4.8 c Description of selected adverse reactions
Severity of adverse effects listed in Section 4.8 b are typically dose dependent.

4.8 d Paediatric Population
BIOGEN MULTIVITAMIN DIABETIC is not recommended for use in children below 18 years of age.

4.8 e Other special populations
Renal impairment: Increases the likelihood of toxicity due to hypermagnesemia and hyperkalemia.

4.9 Overdose
Insufficient reliable information for BIOGEN MULTIVITAMIN DIABETIC overdosage. Side effects listed in section 4.8 can be precipitated and/or be of increased severity.

Overdosage of individual ingredients:
Chromium - Acute chromium toxicity may cause diarrhoea, haemorrhage, vomiting, and blood loss into the gastrointestinal tract resulting in cardiogenic shock.
Iron - Acute overdosage may cause diarrhoea and hematemesis, followed by cardiovascular, liver, or metabolic toxicity, and death.
Long-term overdosage may cause hemosiderosis.
Magnesium - Overdosage may result in CNS depression, confusion, drowsiness, low blood pressure, thirst, loss of tendon reflexes, skeletal muscle paralysis, respiratory depression, cardiac arrhythmias, and, in extreme cases, cardiac arrest, coma, and death.
Manganese - Overdosage might increase the risk of neurotoxicity, including Parkinson-like extrapyramidal symptoms, encephalopathy, and psychosis.
Potassium - Overdosage may result in hyperkalaemia. Symptoms include paraesthesia, weakness, paralysis, listlessness, vertigo, confusion, hypotension, blood in the stool, cardiac arrhythmias, heart block, and death.
Rooibos - Large/long term dosages might cause hepatotoxicity in some patients.
Vitamin A - Overdosage may can cause pseudotumor cerebri, pain, liver toxicity, coma, and even death.
Vitamin B_1, **Vitamin B_2**, **Vitamin B_3**, **Vitamin B_5**, **Vitamin B_6**, **Vitamin B_7**, **Vitamin B_9**, **Vitamin B_{12}**, **Vitamin C**, and **Vitamin E -** Insufficient reliable information.
Vitamin D - Vitamin D toxicity include hypercalcemia, azotaemia, and anaemia.
Zinc - Overdosage may cause irritation and corrosion of the gastrointestinal tract, epigastric pain, watery diarrhoea, and severe vomiting.

Reporting of side effects
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: *https://www.sahpra.org.za/Publications/Index/8*.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
D 34.12 Multiple substance formulation. Complementary Medicine: Health Supplement.

Mechanism of action:

Chromium - Increases insulin sensitivity by activating signalling pathways involved in glucose transporter 4 (GLUT4) translocation.
Iron - Required for oxygen and carbon dioxide transport, functions in the electron transport chain as an electron carrier in cytochromes, plays a role in the Krebs cycle (energy release) and is an essential cofactor in neurotransmitter (dopamine, norepinephrine, and serotonin) synthesis.
Magnesium - Supplementation may improve glycaemic control in patients with type 2 diabetes, by regulating insulin activity or enhancing the action of enzymes involved in glucose utilization.
Manganese - Helps the body to metabolise carbohydrates. The insulin receptor is a hormone-dependent kinase that is stimulated by Manganese.
Potassium - Works jointly with other nutrients to generate beneficial physiological effects.
Rooibos - Unknown.
Vitamin A - B lymphocyte growth, differentiation, and activation (immune function) are dependent on retinol
Vitamin B_1 - Binds with adenosine triphosphate (ATP) to form the coenzyme, thiamine diphosphate, which is required for carbohydrate metabolism.
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.
Vitamin B_3 - Unknown.
Vitamin B_5 - Precursor of coenzyme A (CoA) and acyl carrier protein, is involved in gluconeogenesis; energy release from carbohydrates; fatty acid synthesis/degradation; and the synthesis of sterols, acetylcholine, steroid hormones, porphyrins, and other compounds. Vitamin B_5 also seems to be essential for normal epithelial function.
Vitamin B_6 - Converted to the coenzyme, pyridoxal phosphate, which is involved in a wide variety of metabolic reactions, such as transamination of amino acids, conversion of tryptophan to niacin, synthesis of gamma-aminobutyric acid (GABA) in the CNS, metabolism of serotonin, norepinephrine and dopamine, metabolism of polyunsaturated fatty acids and phospholipids, and the synthesis of the heme component of hemoglobin
Vitamin B_7 - Reduces blood glucose levels by theoretically stimulating the expression of proteins/enzymes that favour hypoglycaemia (insulin, pancreatic glucokinase, and hepatic glucokinase), and inhibiting the expression of hepatic phosphoenolpyruvate carboxykinase (an enzyme stimulating glucose production).
Vitamin B_9 - Unknown.
Vitamin B_{12} - Helps to metabolise carbohydrates, fats and proteins.
Vitamin C - Best known for its antioxidant effects and its role in maintaining proper immune function. It is also involved in several physiological functions such as oxidation-reduction reactions, cellular respiration, catabolism of cholesterol to bile acids, carbohydrate metabolism, lipid and protein synthesis, folic acid to folinic acid conversion, and iron metabolism.
Vitamin D_3 - Vitamin D impacts the function of beta-cells by mediating calcium flux.
Vitamin E - May improve glucose disposal in patients with type 2 diabetes.
Zinc - Increases insulin levels and decreases blood glucose levels.

Pharmacodynamic effects:
Chromium - Trace mineral, may be modestly beneficial for improving glycaemic control in diabetes, especially at higher dosages.
Iron - Trace mineral, stores and transports iron (as myoglobin and hemoglobin) throughout the body.
Magnesium - Chemical element, known to play an essential role in many cellular reactions in the body.
Manganese - Essential nutrient, involved in glucose regulation.
Potassium - Essential element, essential for physiological processes. Inadequate dietary intake of potassium might result in the development of hypertension, stroke, and cardiovascular disease.
Rooibos - Has antioxidant properties which may reduce the risk of type 2 diabetes (T2DM) and its complications.
Vitamin A - Fat-soluble vitamin, contributes to the maintenance of eyesight, skin, membranes and immune function.
Vitamin B_1 - Water-soluble B-complex vitamin, helps to metabolise carbohydrates and is a factor in the maintenance of good health.
Vitamin B_2 - Water-soluble B vitamin involved in vital metabolic processes and is necessary for normal cell growth, function, and energy production.
Vitamin B_3 - Helps metabolizing carbohydrates, fats and proteins and is a good factor in the maintenance of good health.
Vitamin B_5 - Essential B vitamin, helps metabolizing carbohydrates, fats and proteins and is a good factor in the maintenance of good health.
Vitamin B_6 - Member of the Vitamin B family, helps metabolizing carbohydrates, fats and proteins and is a good factor in the maintenance of good health.
Vitamin B_7 - Water-soluble B vitamin serving as a cofactor for biotin-dependent carboxylases which participate in gluconeogenesis (glucose generation), fatty acid synthesis and catabolism.
Vitamin B_9 - Water-soluble B vitamin, is a good factor in the maintenance of good health.
Vitamin B_{12} - Water-soluble B vitamin, is a good factor in the maintenance of good health.
Vitamin C - Antioxidant-rich water-soluble vitamin, for the maintenance of good health.
Vitamin D_3 - Fat-soluble vitamin, for the maintenance of good health.
Vitamin E - Fat-soluble vitamin, for the maintenance of good health.
Zinc - Mineral, may modestly improve glycaemic control in some patients.

5.2 Pharmacokinetic properties

Chromium
Absorption: Only a small percentage (0,4 % - 2,5 %) of chromium is absorbed.
Distribution: Concentrates in the heart, kidney, brain, spleen, muscle, epididymis, testes, and lungs. Serum chromium levels are not equivalent to chromium present in tissue-organ stores.
Metabolism: Once absorbed, chromium is bound to transferrin and concentrated in certain organs.
Excretion: Absorbed chromium is rapidly excreted in the urine. Unabsorbed chromium is excreted in the faeces. Stressors (physical activity, infection, elevated blood sugar, trauma) may increase chromium excretion.

Iron
Absorption: Absorbed in the intestine (predominantly within the duodenum and lesser amounts in the jejunum).
Distribution: Iron is predominantly found in the hemoglobin of red blood cells. The remaining iron is stored in the bone marrow, liver, spleen, or muscle (myoglobin) as ferritin or hemosiderin.
Metabolism: Iron binds to the transport protein, transferrin, which in turn binds to the transferrin receptor complex. Once transferred into cells, Iron can be incorporated into hemoglobin and myoglobin, stored as ferritin, or used to regulate cellular iron metabolism.
Excretion: Body iron is highly conserved. A small quantity of iron is excreted daily, mostly through the feces.

Magnesium
Absorption: Magnesium is absorbed throughout the gastrointestinal tract and requires vitamin D and parathyroid hormone for absorption. Magnesium stores in the body determines the absorption efficiency of magnesium. Plasma concentration of magnesium peaks at 4 hours post supplementation.
Distribution: Magnesium is divided between the skeleton and soft tissue in roughly equal portions. Extracellular magnesium makes up 1 % of total body magnesium. In plasma, ± 30 % magnesium is bound to plasma proteins, 55 % is ionized or free, and 15 % is complexed to anions.
Metabolism: Theoretically, magnesium undergoes a filtration-reabsorption process. Magnesium reabsorption is determined by the presence of parathyroid hormone, plasma magnesium and calcium level alterations, and the use of loop diuretics.
Excretion: Magnesium is primarily excreted via the kidneys (averages 3 % - 5 % of the filtered load). Over a 24-hour period, excretion ranges from 10 - 5 000 mg.

Manganese
Absorption: Absorption rate of manganese from supplements is unknown.
Distribution: Absorbed manganese is present in the blood for a short period. Manganese accumulates in the tissues, including the bone where it can remain for several years.
Metabolism: Unknown.
Excretion: Manganese is cleared via the liver.

Potassium
Absorption: Majority of intestinal potassium absorption occurs in the small intestine, mainly via passive mechanisms.
Distribution: Potassium is distributed in the intracellular and extracellular fluid.
Metabolism: The skeletal muscle and the liver buffer changes in plasma potassium levels via transcellular potassium redistribution and feedback control of renal potassium excretion. When decreased potassium intake is sensed, other homeostatic responses are activated, even when plasma potassium levels are still within the normal range.
Excretion: Approximately 80 % of dietary potassium is recovered in the urine.

Rooibos
Unknown.

Vitamin A
Absorption: Vitamin A is bound to the retinol-binding protein in the plasma. Unesterified retinol is directly absorbed into intestinal cells, predominantly by active transport at lower concentrations and by diffusion at higher concentrations.
Distribution: Vitamin A is stored as retinol, predominantly in the liver.
Metabolism: Vitamin A is metabolized to 11-cis-retinoids and acidic retinoids.
Excretion: Vitamin A is predominantly excreted in the urine. Lesser amounts of vitamin A are lost through the breath and faeces, as inactive metabolites.

Vitamin B_1
Absorption: Vitamin B_1 is absorbed at the proximal part of the small intestine. Smaller dosages are absorbed through active transport, and higher dosages through passive diffusion.
Distribution: Distributed into the heart, skeletal muscle, kidneys, liver, and the brain
Metabolism: Vitamin B_1 is phosphorylated during intestinal uptake. In the human body, vitamin B_1 is predominantly found in its metabolically active form, thiamine diphosphate.
Excretion: Vitamin B1 and its metabolites are excreted in the urine.

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

Vitamin B_3
Unknown.

Vitamin B_5
Absorption: Vitamin B_5 is absorbed in the intestine and delivered directly into the bloodstream by active transport. At higher dosages, passive diffusion may occur.
Distribution: Red blood cells carry vitamin B_5 throughout the body. Vitamin B_5 is predominantly present in the form of coenzyme A (CoA) in the body.
Metabolism: Acts as a precursor for the synthesis of CoA and acyl carrier protein.
Excretion: Vitamin B_5 is excreted in the urine.

Vitamin B_6
Absorption: Passively absorbed in the upper gastrointestinal tract.
Distribution: Unknown.
Metabolism: Vitamin B_6 is converted in the liver to the coenzyme, pyridoxal phosphate.
Excretion: Vitamin B_6 metabolites are excreted in the urine.

Vitamin B_7
Absorption: Biotin is completely absorbed post oral administration. Peak concentration is reached after 1 - 2 hours.
Distribution: The sodium-dependent multivitamin transporter (SMVT) mediates the uptake of biotin into the liver and peripheral tissues, and the reuptake of biotin in the kidneys.
Metabolism: Biotin metabolites are formed by beta-oxidation, sulfur oxidation, or both.
Excretion: Biotin is excreted in the urine as unmetabolized biotin or as the biotin metabolites (biotind, l-sulfoxides, bisnorbiotin methyl ketone, bisnorbiotin, biotin sulfone, and tetranorbiotin-l-sulfoxide).

Vitamin B_9
Absorption: Synthetic vitamin B_9 is almost 100 % bioavailable. Absorption occurs primarily in the duodenum and jejunum.
Distribution: Unknown.
Metabolism: Once absorbed, Vitamin B_9 is reduced to tetrahydrofolate which enters a methylation cycle. Tetrahydrofolate is converted to L-methylfolate.
Excretion: Predominantly excreted in the urine; however, it can also be present in the faeces.

Vitamin B_{12}
Absorption: Vitamin B_{12} binds with intrinsic factor which allows active transportation in the terminal ileum. Vitamin B_{12} can also be passively absorbed, although, to a much lesser extent than active absorption.[13]
Distribution: Unknown
Metabolism: Unknown
Excretion: Half-life of vitamin B_{12} is ± 25 - 30 hours.

Vitamin C
Absorption: Absorption decreases as the dose increases.
Distribution: Predominantly found in the plasma, and to a lesser extent in the lungs, heart, muscle, intestine, kidney, liver and brain.
Metabolism: Vitamin C is transported from the intestines into the blood via the sodium-dependent vitamin C transporter (SVCT1).
Excretion: Absorbed vitamin C is excreted in the urine.

Vitamin B_3
Absorption: Vitamin D is well absorbed in the small intestine.
Distribution: Transported primarily by chylomicron, allowing vitamin D to be distributed to the peripheral tissues. If not absorbed by the peripheral tissue, vitamin D is transported to the liver, where it is converted to calcitriol.
Metabolism: Vitamin D is hydroxylated to the active metabolite, calcitriol, in the liver or kidneys.
Excretion: Vitamin D is predominantly excreted in the faeces.

Vitamin E
Absorption: Vitamin E is absorbed in the small intestine through passive diffusion.
Distribution: Hepatic alpha-tocopherol transfer protein (alpha-TTP) is necessary for the distribution of alpha-tocopherol. Alpha-TTP is present in the spleen, lung, brain, kidney, uterus, and placenta.
Metabolism: Unclear. Vitamin E appears to be a substrate of the cytochrome P450 enzyme system, possibly CYP3A4. In addition, vitamin E also seems to activate a nuclear receptor, pregnane X receptor (PXR), which increases CYP3A4 expression.
Excretion: Vitamin E is primarily excreted via the faeces. The water-soluble metabolites of vitamin E are eliminated in the urine.

Zinc
Absorption: Zinc absorption is increased once zinc deficiency and low zinc intake is sensed. Zinc is predominantly absorbed in the small intestine, particularly the jejunum.
Distribution: More than 85 % of the total zinc in the body is present in the skeletal muscle and bone. Zinc in the plasma is tightly regulated at a concentration of ± 10 - 15 mcmol/L.
Metabolism: Zinc rapidly moves to the liver which maintains systemic zinc homeostasis.
Excretion: Zinc is excreted predominantly in the faeces, with a small amount eliminated in the urine.

5.3 Preclinical safety data (Adults)
Chromium - Likely safe when used orally and appropriately, short-term and possibly safe when used, long-term - upper intake level (UL) not established.
Iron - Likely safe when used orally and appropriately in patients with adequate iron stores, in doses that do not exceed the UL of 45 mg elemental iron daily.
Magnesium - Likely safe when used orally and appropriately in doses below the UL of 350 mg daily.
Manganese - Likely safe when used orally and appropriately in doses below the UL of 11 mg per day.
Potassium - Likely safe when used orally and appropriately - UL not established.
Rooibos - No known information.
Vitamin A - Likely safe when taken in doses below the UL of 3 000 µg per day.
Vitamin B_1 - Likely safe when used orally and appropriately - UL not established.
Vitamin B_2 - Likely safe when used orally and appropriately – UL not established.
Vitamin B_3 - No known information.
Vitamin B_5 - Likely safe when used orally and appropriately - UL not established.
Vitamin B_6 - Likely safe when used orally and appropriately in doses that do not exceed the UL of 100 mg daily.
Vitamin B_7 - Likely safe when used orally and appropriately - UL not established.
Vitamin B_9 - Likely safe when used orally and appropriately in doses below the UL of 1 000 µg.
Vitamin B_{12} - Likely safe when used orally and appropriately - UL not established.
Vitamin C - Likely safe when used orally and appropriately in doses that do not exceed the UL of 2 000 mg.
Vitamin D_3 - Likely safe when used orally long-term, not exceeding the UL of 100 µg daily. Much higher oral dosages, such as 1 250 µg per week for 6-12 weeks are often required for the short-term treatment.
Vitamin E - Likely safe when used orally and appropriately. The UL in healthy individuals is 1 000 mg daily.
Zinc - Likely safe when used orally and appropriately in amounts that do not exceed the UL of 40 mg daily.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
- Magnesium stearate

6.2 Incompatibilities
In the absence of compatibility studies, BIOGEN MULTIVITAMIN DIABETIC must not be mixed with other medicines.

6.3 Shelf Life
23 Months.

6.4 Special precautions for storage
Store in a cool, dry place at or below 25 °C.
Protect from moisture.
Keep the container tightly closed.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents
30's: White, size 00 gelatine capsules are available in a white plastic container sealed with a white plastic screw cap. The container contains a non-edible silica gel sachet and a foam insert.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Biogen
23 Stag Road
Glen Austin
South Africa
Tel: 0860 347 243
Email: info@biogen.co.za
Website: www.biogen.co.za

8. REGISTRATION NUMBER
To be allocated.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Not Applicable.

10. DATE OF REVISION OF THE TEXT
August 2022

333625P01