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BIOGEN
FOR THE RESULTS YOU WANT

MULTIVITAMIN PLUS

PROFESSIONAL INFORMATION

D 33.7 Combination Product. Complementary Medicine

Health supplements are intended only to complement health or supplement the diet.

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

SCHEDULING STATUS: S0

1. NAME OF THE MEDICINE
BIOGEN MULTIVITAMIN PLUS (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each BIOGEN MULTIVITAMIN PLUS tablet contains:		%NRV*
Vitamin A (as Vitamin A palmitate)	69 µgRE	8 %
Beta-carotene (Provitamin A carotenoid)	1 mg	9 %
Lutein (Provitamin A carotenoid) (from Marigold flower)	0,5 mg	2 %
Vitamin B_1 (as Thiamine mononitrate)	12 mg	1000 %
Vitamin B_2 (Riboflavin)	12,5 mg	962 %
Nicotinamide	12,5 mg	78 %
Vitamin B_6 (as Pyridoxine HCl)	12,5 mg	735 %
Folic Acid	200 µg	50 %
Vitamin B12 (Cyanocobalamin)	12,5 µg	521 %
Biotin	30 µg	100 %
Pantothenic Acid	12,5 mg	250 %
Vitamin C (as Ethyl cellulose coated ascorbic acid)	75 mg	75 %
Vitamin D	5 µg	34 %
Vitamin E (dl-alpha tocopheryl acetate)	10 mgTE	67 %
Potassium	5 mg	
Calcium (as Calcium carbonate)	33 mg	3 %
Copper (as Copper sulphate-5-hydrate)	0,1 mg	11 %
Chromium (as Chromium picolinate)	3,8 µg	11 %
Iron (as Ferrous fumarate)	2,3 mg	13 %
Magnesium (as AAC*)	11 mg	13 %
Manganese (as Manganese sulphate)	0,3 mg	11 %
Molybdenum (as AAC*)	5,5 µg	12 %
Selenium (as AAC*)	6,9 µg	13 %
Zinc (as Zinc lactate)	2,8 mg	11 %
PABA (Para-amino benzoic acid)	12,5 mg	
Choline	25 mg	5 %
Inositol	25 mg	
Citrus Bioflavanoids (incl Rutin & Hersperidin)	25 mg	
Kelp (incl. Calcium & Iodine)	2,5 mg	
MSM (Methylsulfonylmethane)	6,25 mg	
Spirulina Powder	50 mg	
Whey protein isolate	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
Tablets (30's/ 60's/180's).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
BIOGEN MULTIVITAMIN PLUS, is a high potency multivitamin and mineral supplement, formulated to provide important micro-nutrients that the average individual struggles to obtain in this day and age.

4.2 Posology and method of administration
Adults and children over 12 years of age:

Posology
Adults: Take 1-2 tablets daily with breakfast, or as recommended by your healthcare provider.

Method of administration
Take BIOGEN MULTIVITAMIN PLUS tablets orally.

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

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

4.3 Contraindications
- Patients with a hypersensitivity to any of the ingredients 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 or haemophiliacs.
- Patients with disturbances of calcium metabolism, e.g. hypercalcaemia, calcium renal calculi or history of renal calculi.

4.4 Special warnings and precautions for use
- Patients with existing bleeding disorders.
- Patients with renal disease, as BIOGEN MULTIVITAMIN PLUS may increase the risk for, or exacerbate kidney disease.
- Patients with hepatic disease, as BIOGEN MULTIVITAMIN PLUS may increase the risk for, or exacerbate liver disease.
- Patients with sarcoidosis, lymphoma, hyperparathyroidism, histoplasmosis, tuberculosis, or those taking vitamin D supplementation.
- Patients with hemoglobinopathies or other refractory anaemias incorrectly diagnosed as iron deficiency anaemia – use with caution.
- Discontinue use at least 2 weeks prior to elective surgical procedures.

4.5 Interaction with other medicines and other forms of interaction
No specific drug interaction studies have been performed on BIOGEN MULTIVITAMIN PLUS as a combination product due to the complexity associated with the number of active ingredients present. However the known interactions of the active ingredients have been summarized.

Interactions with Medicines
- Retinoids:
  The use of vitamin A, as in BIOGEN MULTIVITAMIN PLUS, with retinoids such as isotretinoin and tretinoin, may contribute to hypervitaminosis A.
- Anticoagulants:
  Increased monitoring of INR (International Normalised Ratio) levels is advised when starting or stopping treatment with BIOGEN MULTIVITAMIN PLUS.
- Antibiotics:
  The concomitant use of calcium, iron, magnesium and/or zinc, as in BIOGEN MULTIVITAMIN PLUS, with fluoroquinolones and tetracyclines reduces the absorption of these antibiotics. Advise patients to take these antibiotics 2 to 3 hours before or after taking BIOGEN MULTIVITAMIN PLUS
- Chelating Agents:
  The concomitant use of zinc, as in BIOGEN MULTIVITAMIN PLUS, with penicillamine reduces the absorption of penicillamine. Advise patients to separate doses by 2 to 3 hours.
- Diuretics:
  The use of vitamin D and/or calcium, as in BIOGEN MULTIVITAMIN PLUS, with thiazide diuretics may contribute to hypercalcaemia and milk-alkali syndrome.
- Antiparkinson Agents:
  The effect of levodopa may be reduced by pyridoxine, as in BIOGEN MULTIVITAMIN PLUS, in the absence of dopadecarboxylase inhibitor / carbidopa. The concomitant use of iron, as in BIOGEN MULTIVITAMIN PLUS, and levodopa and / or entacapone may contribute to reduced absorption of these medicines.
- Bisphosphonates:
  The use of calcium, iron and/or magnesium, as in BIOGEN MULTIVITAMIN PLUS, in conjunction with bisphosphonates may contribute to reduced absorption of bisphosphonates. Advise patients to separate doses by 2 to 3 hours.
- Thyroid Agents:
  The concomitant use of iron, as in BIOGEN MULTIVITAMIN PLUS, and levothyroxine sodium may reduce the absorption of levothyroxine from the gastrointestinal tract.
- Antiadrenergics:
  The hypotensive effect of methyldopa may be opposed when used in conjunction with iron, as in BIOGEN MULTIVITAMIN PLUS, due to a reduction in the absorption of methyldopa Immunosuppressants:
  The concomitant use of iron, as in BIOGEN MULTIVITAMIN PLUS, and mycophenolate may reduce the absorption of mycophenolate.

Interactions with Diseases/Impairments
Alcohol decreases the conservation of magnesium via the kidneys, thus increasing the risk for magnesium deficiency. 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 theoretically increases vitamin B_7 catabolism which might cause minor vitamin B_7 deficiency.

4.6 Fertility, pregnancy and lactation
The safety and efficacy of BIOGEN MULTIVITAMIN PLUS in pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use machines
BIOGEN MULTIVITAMIN PLUS 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, Panax ginseng, Vitamin C, Calcium, Magnesium, Vitamin B_3, Vitamin E, Vitamin B_5, Iron, Vitamin B_6 , Vitamin B_2, Vitamin B_1, Retinol (Vitamin A), Copper, Manganese, Folic Acid, Iodine, Biotin, Chromium, Selenium, Vitamin B_{12}, Vitamin D_3 is generally well tolerated when using as prescribed.

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, anxiety 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
The use of BIOGEN MULTIVITAMIN PLUS in children and adolescents has not been established due to lack of adequate data.

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

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
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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.
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.

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 - 5000 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.

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 B1 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 B1 is phosphorylated during intestinal uptake. In the human body, vitamin B1 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 B2 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.
Distribution: Unknown
Metabolism: Unknown
Excretion: Half-life of vitamin B12 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 D_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.

5.3 Preclinical safety data (Adults)
When used orally and appropriately in adults, the ingredients in BIOGEN MULTIVITAMIN is recognized as possibly safe.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
- Magnesium stearate.

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

6.3 Shelf Life
24 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/ 60/ 180 yellow oval shaped tablets are available in a white 175 ml/ 250 ml / 300 ml PET 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
November 2022.