PROFESSIONAL INFORMATION

Category D: Complementary Medicine

Health Supplements. 34.12 Multiple Substance Formulation.

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

SCHEDULING STATUS:

S0

1. NAME OF THE MEDICINE:

GUMMY VITES SELECT SUGAR FREE MULTIVITAMIN (Bear shaped gummies)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 3 g bear shaped gummy contains:	
Ascorbic acid (Vitamin C)	40 mg
dl-α-Tocopheryl Acetate (Vitamin E)	7,5 mg
Nicotinamide (Vitamin B_3)	4 mg
Calcium d-pantothenate (Vitamin B_5)	2,5 mg
Zinc citrate (Zinc)	1 mg
Pyridoxine HCl (Vitamin B_6)	0,85 mg
Folic acid	200 µg
Retinol Acetate (Vitamin A)	200 µg
Potassium Iodide (Iodine)	75 µg
Biotin (Vitamin H)	15 µg
Cyanocobalamin (Vitamin B_{12})	1,2 µg
Cholecalciferol (Vitamin D_3)	200 IU

Sugar free.

Excipient(s) with known effect: None

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Bear shaped gummies.

The bear shaped gummies are strawberry (red) and grape (purple) flavoured.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

A multivitamin and mineral supplement which assists in the:

- Maintenance of good health.
- Development and maintenance of night vision
- Development and maintenance of bones, cartilage, teeth and gums
- Connective tissue formation
- Healing of wounds
- Absorption and use of calcium and phosphorus
- Maintenance of eyesight, skin, membranes and immune function
- Metabolizing of carbohydrates, fats and proteins

And contributes to:

- normal growth and development
- normal red blood cell formation
- absorption and use of calcium and phosphorous
- normal production of the thyroid hormones and normal thyroid function
- Contributes to the reduction of tiredness and fatigue

4.2 Posology and method of administration

Children over the age of 3 years: Chew one (1) bear shaped gummy daily before food.

The gummy should be chewed and not swallowed whole. Do not exceed the recommended dose.

4.3 Contraindications

- Known hypersensitivity to the active substance or to any of the excipients listed under Section 6.1.
- Large doses of Vitamin C may result in hyperoxaluria and the formation of renal calcium oxalate calculi
- Large doses of Vitamin C has resulted in haemolysis in patients with G6PD Deficiency
- Vitamin E might worsen coagulation defects in people with vitamin K deficiency; use cautiously.
- Vitamin E can decrease vitamin K-dependent clotting factors and may exacerbate bleeding disorders; use with caution
- Vitamin B_3 causes vasodilation. Use nicotinamide with caution in patients with unstable angina.
- Vitamin B_3 can interfere with blood glucose control, requiring dosing adjustment of antidiabetic agents.
- There is concern that Vitamin B3 might exacerbate active gallbladder disease; use with caution.
- Vitamin B_3 might exacerbate uncorrected hypotension or orthostatic hypotension; use with caution.
- Supplemental folic acid might exacerbate seizures in people with seizure disorders, particularly in very high doses.
- Excessive doses of vitamin A should be avoided in pregnancy because of potential teratogenic effects
- Chronic alcohol ingestion might potentiate the adverse effects of vitamin A, particularly hepatotoxicity
- Vitamin B_{12} is contraindicated in early Leber disease, which is hereditary optic

nerve atrophy. Vitamin B_{12} can cause severe and swift optic atrophy.

- Vitamin B_{12} is contraindicated in cobalamin or cobalt hypersensitivity.
- Vitamin D should not be given to patients with hypercalcaemia.
- High doses of vitamin D can cause hypercalcemia, which can contribute to arteriosclerosis, particularly in patients with kidney disease

4.4 Special warnings and precautions for use

- Tolerance may be induced with prolonged use of large doses of Vitamin C, resulting in symptoms of deficiency when intake is reduced to normal.
- Prolonged or excessive use of chewable vitamin C preparations may cause erosion of tooth enamel
- Vitamin C may increase the absorption of iron in iron-deficiency states.
- Long-term use of large doses of vitamin B_6 is associated with the development of severe peripheral neuropathies
- Enhanced susceptibility to the effects of vitamin A may be seen in children and in patients with liver disease.
- Gastrointestinal absorption of vitamin A may be impaired in cholestatic jaundice and fat-malabsorption conditions.
- People receiving haemodialysis or peritoneal dialysis might require increased biotin supplementation. Haemodialysis and/or peritoneal dialysis might increase biotin excretion and deplete the body's biotin stores.
- People who smoke might require increased biotin supplementation.
- Excessive intake of vitamin D leads to the development of hyperphosphatemia or hypercalcaemia.
- Prolonged use of high doses of zinc supplements, orally or parenterally, leads to copper deficiency with associated sideroblastic anaemia and neutropenia
- Long-term excessive alcohol consumption is associated with impaired zinc absorption and increased excretion of zinc in the urine.
- Patients over the age of 45 years or with nodular goitres are especially

susceptible to hyperthyroidism when given iodine supplementation.

- Folic acid can mask pernicious anaemia by decreasing megaloblastic anaemia. This can prevent appropriate treatment with Vitamin B_{12} and result in neurological damage. Patients should be warned to avoid treating undiagnosed anaemia with folic acid.
- Intestinal infections and infestations can reduce oral vitamin A absorption.
- Iron deficiency may impair the metabolism of vitamin A
- Vitamin D should be used with caution in infants, who may have increased sensitivity to its effects, and patients with renal impairment or calculi, or heart disease, who might be at increased risk of organ damage if hypercalcaemia occurred.
- Vitamin D may increase calcium levels in people with histoplasmosis, hyperparathyroidism, lymphoma, sarcoidosis and tuberculosis.

4.5 Interaction with other medicines and other forms of interaction

Interactions with medicines

Alcohol: Concomitant use of alcohol and Vitamin B_3 might increase the risk of flushing and hepatotoxicity.

Alpha-Lipoic Acid: Taking biotin with alpha-lipoic acid may reduce biotin or alpha-lipoic acid absorption

Amiodarone: Amiodarone contains 37.3% iodine and can increase iodine levels.

Anticoagulant/Antiplatelet Drugs: Concomitant use of vitamin E and anticoagulant or antiplatelet agents might increase the risk of bleeding.

Vitamin B_3 may increase the risk of bleeding in some patients.

Antidiabetic drugs: Vitamin B_3 can increase blood glucose levels and may diminish the effects of antidiabetes drugs.

Antithyroid Drugs: Concomitant use of antithyroid drugs with iodine may result in additive hypothyroid activity, and may cause hypothyroidism

Bile acid sequestrants: Bile acid sequestrants can bind Vitamin B_3 and decrease absorption. Separate administration by 4-6 hours to avoid an interaction.

Calcium/ magnesium: Vitamin D may increase the absorption of calcium/magnesium.

Chromium: Chromium and zinc might impact each other's absorption.

Copper, fluoroquinolones, iron, penicillamine, and tetracyclines: Zinc supplements reduce the absorption of these drugs

Estrogens: Vitamin C increases plasma estrogen levels when taken concurrently with oral contraceptives or hormone replacement therapy, including topical products

Fluphenazine: Vitamin C might decrease levels of fluphenazine

Levodopa: Vitamin B_6 reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given.

Lithium: Lithium can inhibit thyroid function. Concomitant use with iodine may have additive or synergistic hypothyroid effects

Magnesium: Magnesium and zinc can interfere with each other's absorption

Methotrexate: Methotrexate exerts its cytotoxic effects by preventing conversion of folic acid to the active form needed by cells.

Omeprazole: Affects the bioavailability of vitamin C.

Phenobarbital: Folic acid can have direct convulsant activity in some people, reversing the effects of phenobarbital and worsening seizure control. It also reduces serum folate levels.

Phenytoin/Phenobarbital: Vitamin B_6 has been reported to decrease serum concentrations of these drugs.

Phenytoin: Folic acid may be a cofactor in phenytoin metabolism. Folic acid can reduce serum levels of phenytoin in some patients.

Thiazide Diuretics, Calcium, or Phosphate: Increased risk of hypercalcaemia if vitamin D is given with these drugs.

Vitamin A: Zinc might increase vitamin A absorption.

Vitamin B_5: Taking biotin with vitamin B_5 may reduce biotin or vitamin B_5 absorption.

Warfarin: High doses of vitamin C may reduce the response to warfarin, possibly by causing diarrhoea and reducing warfarin absorption

Nutrient depletion:

Nutrient	***Medicine/substance***
Vitamin C	Alcohol, Aspirin, Calcium Channel Blockers, Diuretic Drugs, Estrogens, Proton Pump Inhibitors (PPIs).
Vitamin E	Bile Acid Sequestrants, Carbamazepine, Chemotherapy, Gemfibrozil, Mineral Oil, Orlistat, Phenytoin, Phenobarbital
Vitamin B_3	Beta-Carotene, Selenium, Vitamin C, Vitamin E, Azathioprine, Chloramphenicol, Cycloserine, 5 – Fluorouracil, Isoniazid, Levodopa/Carbidopa, Mercaptopurine, Phenytoin, Valproate
Vitamin B_5	Antibiotic Drugs
Vitamin B_6	Antibiotic Drugs, Cycloserine, Furosemide, Estrogens, Hydralazine, Isoniazid, Penicillamine, Theophylline
Folic acid	Alcohol, Aminosalicylic Acid, Antacids, Antibiotic Drugs, Antiepileptics, Antituberculous drugs, Aspirin, Carbamazepine, Cholestyramine, Colestipol, Cycloserine, Diuretic Drugs, Estrogens, H_2 Blockers, Glucarpidase, Folic acid antagonists (Methotrexate, Pyrimethamine, Triamterene, Trimethoprim, Sulfonamides), Metformin, Methotrexate, Methylprednisolone, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), Oral contraceptives, Pancreatic Enzymes, Phenobarbital, Phenytoin, Primidone, Proton Pump Inhibitors (PPIs), Retinoids, Sulfasalazine, Valproate.
Vitamin A	Bile Acid Sequestrants, Estrogens, Liquid Paraffin Mineral Oil, Neomycin, Orlistat
Biotin	Antibiotic Drugs, Carbamazepine, Phenobarbital, Phenytoin, Primidone

Vitamin B_{12}	Aminosalicylic Acid, Antibiotic Drugs, Aspirin Colchicine, Bile Acid Sequestrants, H_2-Blockers, Metformin, Neomycin, Nitrous Oxide, Contraceptive Drugs, Anticonvulsants, Proton Pump Inhibitors (PPIs), Zidovudine.
Vitamin D	Carbamazepine, Cholestyramine, Colestipol, Efavirenz, Isoniazid, Mineral Oil, Orlistat, Phenobarbital, Phenytoin, Primidone, Rifampicin, Stimulant Laxatives, Sunscreens, Cimetidine, Heparin, Low Molecular Weight Heparins (LMWHs)
Zinc	Calcium Supplements, Captopril, Cholestyramine, Cisplatin, Corticosteroids, Disulfiram, Estrogens, Ethambutol, H_2-Blockers, Iron Supplements, Pantoprazole, Penicillamine, Phenytoin, Phosphorus-Containing Preparations, Propofol, Proton Pump Inhibitors (PPIs), Quinolone Antibiotics, Tetracycline Antibiotics, Thiazide Diuretics, Valproate, Zidovudine.
Iodine	Metronidazole

Nutrient accumulation:

Nutrient	***Medicine/substance***
Vitamin A	Synthetic retinoids

Interactions with laboratory tests

Vitamin C, a strong reducing agent, interferes with laboratory tests involving oxidation and reduction reactions.

Catecholamines: Vitamin B_3 can falsely increase some urinary catecholamine fluorometric assay results. Vitamin B_3 produces fluorescent substances in the urine, which can falsely elevate test results.

Glucose: Vitamin B_3 can cause a false-positive reaction with urine glucose tests which rely on cupric sulphate solution (Benedict's reagent).

Vitamin B_{12} can cause a false-positive test result for intrinsic factor antibodies.

Avoid using powdered gloves when drawing blood for *zinc* assays, due to potential

for sample contamination.

Iodine and iodides can affect the thyroid gland, their use may interfere with tests of thyroid function.

Interactions with food

Vitamin E absorption requires the presence of fat to allow for solubilization and incorporation into micelles.

Hot drinks: Vitamin B_3-induced flushing and itching might be increased if taken with a hot drink.

Dietary fat increases *vitamin A* absorption.

Raw egg white contains avidin, a protein which binds *biotin* in the intestine and prevents biotin absorption

Excessive alcohol intake lasting longer than two weeks can decrease *vitamin* B_{12} absorption from the gastrointestinal tract.

Coffee might reduce *zinc* absorption.

4.6 Fertility, pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

No fertility data available.

4.7 Effects on ability to drive and use machines

GUMMY VITES SELECT SUGAR FREE MULTIVITAMIN is unlikely to influence your child's ability to pay attention.

4.8 Undesirable effects

Frequency unknown:

Metabolism and nutrition disorders: Decreased serum folic acid concentrations, loss of appetite

Psychiatric disorders: somnolence, tremor

Nervous system disorders: fever, chills, malaise

Ear and labyrinth disorders: nausea, dizziness

Vascular disorders: headache, paraesthesia, hot flushing

Gastrointestinal disorders: vomiting, abdominal pain, heartburn, diarrhoea, gastrointestinal disturbances, metallic taste, thirst, constipation

Skin and subcutaneous tissue disorders: Allergic hypersensitivity reactions, Acneform and bullous eruptions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions of GUMMY VITES SELECT SUGAR FREE MULTIVITAMIN is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to the Adcock Ingram Pharmacovigilance department by e-mail to Adcock.Aereports@adcock.com, fax to +27 86 553 0128 or call 011 635 0134. Alternatively, it can be reported to the South African Health Products Regulatory Authority (SAHPRA) via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9. Overdose

See section 4.8, Undesirable effects.

In overdose, side effects can be precipitated and/or be of increased severity.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

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Mechanism of action

Vitamin C has a role in several physiological functions and a variety of metabolic processes.

The major function of **vitamin E** is probably that of a chain-breaking antioxidant that prevents the formation of free radicals

Vitamin B_3 is a precursor of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). These coenzymes are essential for oxidation-reduction reactions, ATP synthesis, and ADP-ribose transfer reactions.

Vitamin B_5 is a component of coenzyme A which is essential in the metabolism of carbohydrate, fat, and protein.

Vitamin B_6 is required for amino acid metabolism. It is also involved in carbohydrate and lipid metabolism.

Folic acid-based coenzymes play a major role in intracellular metabolism and an indirect role in the rate-limiting step of DNA synthesis.

Vitamin A is required for vision, growth and bone development, reproduction, cell proliferation and differentiation, immune function, and the integrity of mucosal and epithelial surfaces.

Biotin-containing enzymes are involved in gluconeogenesis, fatty acid synthesis, propionate metabolism, and the catabolism of leucine in mammals

Vitamin B_{12} is required for nucleoprotein and myelin synthesis, cell reproduction, normal growth, and normal erythropoiesis.

The main function of **vitamin D** is to regulate serum calcium and phosphorus concentrations.

Zinc is a cofactor in many biological processes including DNA, RNA, and protein synthesis. Zinc also plays a role in immune function, wound healing, reproduction, growth and development, behaviour and learning, taste and smell, blood clotting, thyroid hormone function, and insulin action.

Iodine comprises 65% of thyroxine (T_4) and 59% of triiodothyronine (T_3). These

iodine-rich thyroid hormones control many biochemical reactions, particularly protein synthesis and enzymatic processes

5.2 Pharmacokinetic properties

Vitamin C is well absorbed orally at lower does, but absorption decreases as the dose increases. Most vitamin C that is absorbed is excreted in the urine.

Absorption of all forms of **vitamin E** takes place mostly in the small intestine by passive diffusion. Vitamin E is dependent on hepatic dl-α-Tocopheryl transfer protein (alpha-TTP) for distribution. Vitamin E is eliminated is primarily unchanged via faeces.

Vitamin B_3 is water-soluble and well-absorbed when taken orally. It is metabolized in the liver to nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which are essential for oxidation-reduction reactions, ATP synthesis, and ADP-ribose transfer reactions.

Vitamin B_5 is readily absorbed from the gastrointestinal tract after oral doses. It is widely distributed in the body tissues and appears in breast milk. About 70 % of pantothenic acid is excreted unchanged in the urine and about 30 % in the faeces.

Vitamin B_6 is absorbed passively in the upper gastrointestinal tract. In the liver, Vitamin B_6 is converted to the coenzyme pyridoxal phosphate. Vitamin B_6 metabolites are excreted in the urine.

Folate in food is about 20 % to 50 % less bioavailable than synthetic folic acid, which is almost 100 % bioavailable. Before folate from food can be absorbed, the polyglutamate side chain must undergo enzymatic deconjugation in the small intestine to form the absorbable monoglutamate form. After folic acid is absorbed, it is reduced to tetrahydrofolate and then enters a methylation cycle. Tetrahydrofolate is then converted to L-methylfolate. Folic acid is excreted mainly in the urine; however, it is also found in the faeces. Folate is also lost during hemodialysis.

In the plasma, **vitamin A** is bound to retinol-binding protein. Dietary retinyl esters are hydrolyzed by pancreatic and intestinal enzymes. The liver seems to maintain

vitamin A concentrations within a relatively narrow range by storage and release of vitamin A. Ingested vitamin A is stored in the body as retinol, predominantly in the liver, but also in the retina, kidneys, lungs, adrenal glands, and intraperitoneal fat. In the body, vitamin A is metabolized to 11-cis-retinoids and acidic retinoids. The majority of vitamin A is excreted in the urine.

After oral administration, **biotin** is completely absorbed and reaches peak concentration after 1-2 hours. However, dietary biotin is bound to lysine residues of protein. Before it can become bioactive, it must be cleaved by biotinidase from food proteins. After being cleaved, biotin is transported across the intestinal lumen enterocytes by the sodium-dependent multivitamin transporter (SMVT) and into the liver and peripheral tissues. Biotin metabolites are formed by beta-oxidation, sulphur oxidation, or both. About half of the dose of biotin is excreted within 24 hours. Biotin is recycled endogenously.

Vitamin B12 is absorbed via an active transport mechanism in the terminal ileum. This requires the glycoprotein, intrinsic factor, which is produced by the stomach. At normal gastric pH, vitamin B12 is cleaved from proteins in food. It then binds to intrinsic factor and is absorbed by ileal transport. Orally, vitamin B12 as cyanocobalamin and cyanocobalamin-SNAC has a half-life of about 25-30 hours.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

- Water
- Agar agar [E406]
- Carnauba wax [E 903]
- Chicory root fibers

- Pectin [E440],
- Tapioca starch [E 1404]
- Trisodium citrate [E 331]
- Berries (strawberry) flavour (natural)
- Colourant (black carrot concentration)
- Colourant (Chlorophyll) [E 140]
- Grape flavour (natural)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep in a cool and dry place.

6.5 Nature and contents of container

60 gummies in a clear PET bottle with a white lid packed in a unit carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road,

Erand Gardens,

Midrand

1685

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)

To be allocated.

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Not Applicable.

10. DATE OF REVISION OF THE TEXT

8 September 2022

adcock ingram