CAL-C-VITA® COMBO is a Health Supplement. **D: Complementary Medicine**

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

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

CAL-C-VITA® COMBO Effervescent tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains:

Name of ingredients	**Quantity**
Vitamin C	1000 mg
Zinc	10 mg

Contains sugars: Sorbitol 655 mg

Contains sweeteners: Acesulfame Potassium 20 mg and Aspartame* 20 mg

*Phenylketonurics: Contains a source of phenylalanine

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Effervescent tablets.

Light orange tablet with bevelled edges and flat faces

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Cal-C-Vita® Combo is a combination of high strength vitamin C and Zinc. Both vitamin C and zinc are independently essential for the defence potential and disease resistance mechanisms of the body:

- Common cold
- Immune support

4.2. Posology and method of administration

Adults and children over 12 years: 1 effervescent tablet a day dissolved in a glass of water.

4.3. Contraindications

Hypersensitivity to any of the active substances or to any of the excipients listed in section 6.1.

Patients suffering from or having a history of Nephrolithiasis must not take this product. Patients suffering from oxalate urolithiasis or oxaluria must not take this product.

Patients suffering from severe renal insufficiency or renal failure must not take the product. This includes patients on dialysis.

Patients suffering from Hemochromatosis must not take this product.

4.4. Special warnings and precautions for use

Patients suffering from renal insufficiency should consult a physician or healthcare professional prior to intake of large doses of ascorbic acid (see section 4.9).

Do not exceed the recommended doses. Acute or chronic overdose (> 2 g / day) increases risk of adverse effects including formation of calcium oxalate deposits, acute tubular necrosis, and/or renal failure (see section 4.9).

Patients suffering from glucose-6-phosphatase deficiency should not take higher than the recommended dose. Overdose of vitamin C in this patient population has been associated with hemolytic anemia (see section 4.9).

Patients receiving other single vitamins or multivitamin preparations, any other medication or those under medical care must consult a health care professional before taking this product (see sections 4.5 and 4.9).

Separate the intake of the product from other medication by 4 hours unless otherwise specified (see section 4.5).

Vitamin C may interfere with laboratory tests resulting in false readings. Inform your physician when taking this product and diagnostic measures are planned or done.

Vitamin C may interfere with test kits and meters measuring glucose levels resulting in false results. Please check the package insert of the test kit or meter for guidance (see section 4.5).

Cal-C-Vita® Combo contains a source of phenylalanine. Therefore, may be harmful to people with phenylketonuria.

Cal-C-Vita® Combo contains 166 mg sodium per tablet. This should be taken into consideration by patients on a controlled sodium diet.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5. Interactions with other medicines and other forms of interaction

Medicine interactions

Active ingredient	Medicine	Description
Ascorbic acid	Desferrioxamine	Vitamin C may enhance tissue iron toxicity, especially in the heart, causing cardiac decompensation
	Cyclosporine	Vitamin C may reduce cyclosporine blood levels
	Indinavir	High dose of vitamin C significantly reduces the serum concentration of indinavir, which may interfere with the effectiveness of Indinavir

	Disulfiram	Chronic or high doses of Vitamin C may interfere with the effectiveness of disulfiram
	Warfarin	High doses of Vitamin c may interfere with the effectiveness of Warfarin
Zinc		Zinc forms complexes with certain substances (including tetracycline antibiotics, quinonolone antibiotics, penicillamine) resulting in decreased absorption of both substances. As these interactions occur in the gastro-intestinal tract, the potential for interaction should be reduced by taking the product separately from other drugs. It is usually sufficient to separate the intake by at least 2 hours before or 4-6 hours after ingestion of the other drug, unless otherwise specified

Food interactions:

Iron:

Vitamin C may enhance iron absorption, especially in individuals with iron deficiency. Small incremental increases of iron could be important in subjects with conditions such as hereditary hemochromatosis or in subjects heterozygous to this condition, as it may exacerbate iron overload.

Zinc bioavailability may be reduced by high concentrations of ferrous ions in iron supplements. The interaction becomes insignificant when the supplements are taken with food.

Copper:

Zinc may reduce copper absorption.

Lab interactions:

As vitamin C is a strong reducing agent, it can cause chemical interference in laboratory tests that involve oxidation-reduction reactions, such as the analyses of glucose, creatinine, carbamazepine, uric acid, and inorganic phosphates in urine, serum and of occult blood in feces. Using specific tests that are not dependent on reducing properties or discontinuing extra dietary vitamin C will avoid any undesirable interference. Refer to the manufacturer's information to determine if vitamin C interferes with the test. Vitamin C may interfere with tests that measure urinary and blood glucose resulting in false readings, although it has no effect on blood glucose levels. Please refer to the package insert of the meter or testing kit to determine if vitamin C interferes and guidance for accuracy in readings.

4.6. Fertility, pregnancy and lactation

Fertility:

To date there is no evidence suggestive that vitamin C and/or Zinc causes adverse reproductive effects in humans

Pregnancy:

Cal-C-Vita® Combo is considered generally safe for use during pregnancy when used as labelled.

The product should only be used in pregnancy when clinically indicated and recommended by a doctor or healthcare professional.

The labelled dose should not be exceeded since chronic overdose might be harmful to the foetus and neonate.

Lactation:

The vitamin and mineral are excreted in to the breastmilk, this should be taken into consideration, especially if the infant is receiving any other supplements.

4.7. Effects on ability to drive and use machines

Cal-C-Vita® Combo has no or negligible influence on the ability to drive and use machines

4.8. Undesirable effects

Cal-C-Vita® Combo may have some undesirable effects.

The following undesirable effects have been reported and the frequencies are unknown.

Gastrointestinal disorders

Diarrhoea, nausea, vomiting, gastrointestinal and abdominal pain

Immune System Disorders

Allergic reaction, anaphylactic reaction, anaphylactic shock.

Hypersensitivity reactions with respective laboratory and clinical manifestations include allergic asthma syndrome, mild to moderate reactions potentially affecting skin, respiratory tract, gastrointestinal tract and cardiovascular system, including symptoms such as rash, urticaria, allergic oedema and angioedema, pruritus, cardio-respiratory distress, and, severe reactions, including anaphylactic shock have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicine 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 SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9. Overdose

Vitamin C:

Acute or chronic overdose of vitamin C may significantly elevate serum and urinary oxalate levels. In some instances, this may lead to hyperoxaluria, calcium oxalate crystalluria, calcium oxalate deposition, kidney stone formation, tubulointerstitial nephropathy, and acute renal failure. Individuals with mild to moderate renal insufficiency may be susceptible to these effects of vitamin C toxicity at lower doses and should consult a health care professional before use of the product.

Overdose of vitamin C may result in oxidative haemolysis or disseminated intravascular coagulation in patients with glucose-6-phosphate dehydrogenase deficiency.

Zinc:

Zinc overdose can cause irritation and corrosion of the gastrointestinal (GI) tract, acute renal tubular necrosis, interstitial nephritis, copper deficiency, sideroblastic anaemia, and myeloneuropathies.

If overdose with the product is suspected, intake should be stopped, and a health care professional consulted for treatment of clinical manifestations. Vitamin C is removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Vitamin C

Ascorbic acid is an important water-soluble vitamin and antioxidant. Due to the low storage capacity of the body for vitamin C, a regular intake of sufficient amounts is essential to humans.

Ascorbic acid and its metabolite dehydroascorbic acid form a reversible redox system that is involved in many enzymatic reactions and forms the basis for the spectrum of action of vitamin C. Ascorbic acid functions as a cofactor in a number of hydroxylation and amination reactions by transferring electrons to enzymes that provide reducing equivalents.

The importance of ascorbic acid to the human body is most clearly evident in clinically manifest vitamin C deficiency, i.e. scurvy. Ascorbic acid plays a key role in the production of hydroxyproline from proline, which in turn is essential to the development of functionally active collagen. The symptoms seen in scurvy, such as delayed wound healing, disturbances of bone growth, vascular fragility, and disorders of dentine formation, are the result of impaired collagen formation.

Zinc

As with vitamin C, low levels of zinc may also adversely affect the healing rate of wounds, ulcers and decubitus.

Zinc status is of major importance in maintenance of effective immune response, particularly T-cell-mediated response

5.2. Pharmacokinetic properties

Absorption:

Ascorbic acid is absorbed primarily in the upper part of the small intestine via sodium-dependent active transport.

When ascorbic acid is present in high concentrations, uptake occurs by means of passive diffusion. After oral administration of doses of 1-12 g, the proportion of ascorbic acid absorbed falls from approximately 50% to about 15%, though the absolute quantity of substance taken up continues to increase.

Zinc is absorbed all along the small intestine. The absorption of zinc (ionic) administered in solution on an empty stomach ranges from 41-79%, while the zinc present in foods or that given as a supplement with meals is absorbed in the range of 10-40%.

Distribution: The physiological body pool of vitamin C is about 1500 mg. Plasma protein binding of ascorbic acid is approximately 24%. Serum concentrations are normally 10 mg/l (60 µmol/l). Concentrations below 6 mg/l (35 µmol/l) indicate that the intake of vitamin C is not always adequate, and concentrations below 4 mg/l (20 µmol/l) indicate that the intake is actually inadequate. In clinically manifest scurvy, serum concentrations are below 2 mg/l (10 µmol/l).

Total body zinc content is controlled in part by regulating the efficiency of intestinal absorption and the excretion from endogenous zinc pools to maintain zinc homeostasis. The adult total body zinc content ranges from about 2.3 mmol (1.5 g) in women to 3.8 mmol (2.5 g) in men. Zinc is present in all organs, tissues, fluids, and secretions of the body. Zinc is primarily an intracellular ion, with well over 95% of the total-body zinc found within cells. Zinc is associated with all organelles of the cell, but about 60 to 80% of the cellular zinc is found in the cytosol.

Metabolism: Ascorbic acid is metabolised partly via dehydroascorbic acid to oxalic acid and other products. When ingested in excessive quantities, however, ascorbic acid is largely excreted in unchanged form in the urine and faeces. Ascorbic-acid-2-sulphate also appears as a metabolite in the urine.

The total amount of zinc present in the major tissues is much larger than the total in plasma. Thus, relatively small variations in zinc content of tissues, such as the liver, can have dramatic effects on the plasma zinc. All absorbed zinc passes through the plasma to the tissues, and the flux of zinc through the plasma is said to be replaced approximately 130 times per day. There is no specific zinc “store”. Human experimental studies with low-zinc diets 2.6-3.6 mg/day /40-55 mmol/day) have shown that circulating zinc levels and activities of zinc-containing enzymes can be maintained within normal range over several months highlighting the efficiency of the zinc homeostasis mechanism.

Elimination: The physiological body pool of ascorbic acid is about 1500 mg. The elimination half-life of ascorbic acid depends on the route of administration, the quantity administered and the rate of absorption. Following an oral dose of 1 g the half-life is about 13 hours. When 1-3 g vitamin C /day is taken, the main route of excretion is renal. With doses exceeding 3 g, increasing quantities are excreted unchanged in the faeces.

The major route for endogenous zinc excretion is into the gastrointestinal tract with ultimate loss in the faeces. When tracer doses of zinc are given either orally or intravenously, only about 2 to 10% is recovered in the urine; the remainder is lost in the faeces. In humans, endogenous faecal losses may range from <15 µmol/day (1 mg/day) with extremely low intakes to over 80 µmol/day (5 mg/day) with extremely high intakes. Normally, about 6 to 9 µmol (400 to 600 µg) of zinc is excreted daily in the urine.

5.3. Preclinical safety data

No specific study with this product was done, but the active ingredients of Cal-C-Vita Combo are well known.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium hydrogen carbonate, sodium carbonate anhydrous, citric acid anhydrous, sorbitol, aspartame, acesulfame potassium, sodium chloride, orange flavour, tangerine flavour and beta-carotene

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 Months

6.4. Special precautions for storage

Store at or below 25 °C

Keep the tube tightly closed in order to protect from moisture

Store in the original package in order to protect from moisture

Keep out of reach of children

6.5. Nature and contents of container

10, 15, 20 or 30 effervescent tablets in polypropylene tube closed by a PE stopper containing a desiccant.

Box of one or two tubes containing 10 or 15 tablets

6.6. Special precautions for disposal and other handling.

Not applicable

7. HOLDER OF CERTIFICATE OF REGISTRATION

Bayer (Pty) Ltd.

27 Wrench road

Isando

1600

South Africa

Co Reg. no.: 1968/011192/07

Tel: +27 11 921 5000

8. REGISTRATION NUMBERS

To be allocated

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of registration: To be allocated

10. DATE OF REVISION OF THE TEXT