Not to be sold by retail without the prescription of a Registered Medical Practitioner

1. Generic Name

Ascorbic Acid (Vitamin C) and Zinc Chewable Tablets
(Brand Name: Bluvit®-CZ Chewable Tablets)

2. Qualitative and Quantitative Composition

Each Uncoated Chewable Tablet Contains:
Ascorbic Acid IP ……..… 100 mg.
Sodium Ascorbate IP ……..……... 450 mg.
(Equivalent to Ascorbic Acid …….…….. 400 mg)
Zinc Citrate USP equivalent to Elemental Zinc ……..... 5 mg.
Excipients……..…. q.s.
Colour: Sunset Yellow FCF.

3. Dosage Form and Strength

Dosage Form: Chewable Tablets.
Dosage Strength: Ascorbic Acid 100 mg, Sodium Ascorbate 450 mg, and Zinc Citrate 5 mg per tablet.

4. Clinical Particulars

4.1 Therapeutic Indication

BLUVIT-CZ tablets are indicated for the prevention and treatment of Vitamin C deficiency, including scurvy. BLUVIT-CZ Tablets are also useful in boosting immunity and reducing duration and severity of cold symptoms.

4.2Posology and Method of Administration

Adults and adolescents: 1 tablet once or twice daily.
Children between 6 to 12 years: 1 tablet once daily.
Chew or crush tablets completely before swallowing. Do not swallow the whole tablet.
Or, as directed by the physician.

4.3Contraindications

BLUVIT-CZ Tablets are contraindicated in the following:

- Known hypersensitivity to Vitamin C, Zinc or to any component of the formulation.
- Iron storage diseases (thalassaemia, haemochromatosis, sideroblastic anaemia) or other medical conditions that predispose individuals to iron overload.
- Patients with hyperoxaluria.

4.4Special Warnings and Precautions for Use

Ascorbic Acid

Exceeding the recommended dose should be avoided as there have been isolated reports of severe haemolysis in patients with erythrocytic glucose-6-phosphate dehydrogenase deficiency when taking high doses (> 4000 mg/day) of ascorbic acid. Do not exceed the recommended dose.
Caution is required and use the minimum recommended dose in patients with renal impairment.

Zinc
Long-term, excessive alcohol drinking is linked to poor zinc absorption in the body.
Large doses of zinc can lower blood sugar in people with diabetes. People with diabetes should use zinc-containing products cautiously.
Avoid taking zinc with foods that are high in calcium or phosphorus, as it may cause decrease in absorption of zinc.

4.5Drug Interactions

Ascorbic Acid
Iron: Administration of ascorbic acid leads to increased absorption of iron from the gastrointestinal tract.
Deferoxamine: Concurrent administration of ascorbic acid with deferoxamine enhances urinary iron excretion. Cases of cardiomyopathy and congestive heart failure have been reported in patients with idiopathic haemochromatosis and thalassaemias receiving deferoxamine who were subsequently given ascorbic acid. In early treatment, when there is excess tissue iron, there is some evidence that ascorbic acid may worsen iron toxicity, particularly to the heart.
Antacids: Ascorbic acid may increase gastrointestinal absorption of aluminium. Concomitant administration of aluminium-containing antacids may affect urinary aluminium elimination. Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.
Aspirin: Concomitant administration of acetylsalicylic acid and ascorbic acid may interfere with absorption of ascorbic acid. Renal excretion of salicylate is not affected and does not lead to reduced anti-inflammatory effects of aspirin.

Zinc
Penicillamine: Zinc decreases absorption of penicillamine and thus decrease the effectiveness of penicillamine. Zinc and penicillamine should be taken at least 2 hours apart.
Antibiotics (cephalexin, quinolones, and tetracyclines): Zinc might decrease absorption of antibiotics in the body. Administration of zinc along with some antibiotics might decrease the effectiveness of these antibiotics. Antibiotics should preferably be taken at least 2 hours before or 4 hours after zinc usages.
Anti-diabetic drugs: Zinc might decrease blood sugar in people with type 2 diabetes. Diabetes medications are also used to lower blood sugar. Taking zinc along with anti-diabetic drugs might cause hypoglycemia.
Cisplatin: Taking zinc along with cisplatin may increase the effects and side effects of cisplatin.

Others: The drugs such as warfarin, methyl testosterone, and risedronate can interact with zinc become less effective.

4.6Use in Special Populations

Pregnant Women

For ascorbic acid no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. BLUVIT-CZ Tablets can be administered in pregnant women. It is recommended not to exceed the stated doses during pregnancy. The tolerable upper intake level (UL) of ascorbic acid and zinc in pregnancy is 2000 mg/day and 40 mg/day respectively.

Lactating Women

Ascorbic acid is excreted in breast milk. BLUVIT-CZ Tablets can be administered during lactation. It is recommended not to exceed the stated doses during lactation. The tolerable upper intake level (UL) of ascorbic acid and zinc during lactation is 2000 mg/day and 40 mg/day respectively.

Paediatric Patients

BLUVIT-CZ Tablets are not recommended for use in children under 6 years. In children above 6 years of age, one BLUVIT-CZ Tablet can be administered once daily. The tolerable upper intake level (UL) of ascorbic acid and zinc in children above 6 years is 650 to 1200 mg/day and 23 to 34 mg/day respectively.

Geriatric Patients

The usual adult dose can be administered in the elderly population provided that the renal function is normal.

4.7Effect on Ability to Drive and Use Machines

On the basis of the product's pharmacodynamic profile and reported adverse events, ascorbic acid and zinc have no known effect on an individual's ability to drive or operate machinery. However, if affected by dizziness following use of this product, patient should be advised not to drive or operate machinery.

4.8Undesirable Effects

Adverse effects that might occur with BLUVIT-CZ Tablets include allergic reactions, including hypersensitivity reactions (such as shortness of breath, swelling of the face and skin rash), headache, dizziness, diarrhoea, nausea, vomiting, dyspepsia, upset stomach, abdominal pain, fatigue, metallic taste, pink or bloody urine, side or lower back pain, flushing or redness of the skin.

4.9Overdose

Ascorbic Acid

Occasionally transient osmotic diarrhoea may occur in doses over 3 g and almost always at doses above 10 g. There is a risk of haemolysis and kidney stones being formed if high doses of ascorbic acid are taken.

Zinc

Excessive intake of zinc greater than 100 mg daily from all sources can depress the immune system and become toxic. This may also lead to copper-deficiency anemia and reduced high density lipoprotein (HDL) cholesterol levels.

5. Pharmacological Properties

5.1 Mechanism of Action

Ascorbic Acid - Antioxidant Effect

Ascorbic acid is an antioxidant agent (electron donor or reducing agent). Antioxidants inhibit oxidation and block damage caused by free radicals to the cells and tissues. Free radicals are produced inside the body by oxidation process when body breaks down food or when body exposed to tobacco smoke or radiation. The build-up of free radicals over time is largely responsible for the aging process. When free radicals accumulate, they can promote oxidative stress, which has been linked to many chronic diseases such as heart diseases, arthritis, cancer, etc.

Vitamin C acts as scavengers to free radicals. Being antioxidant, vitamin C protects cells from harmful effects of free radicals and reduces the risk of chronic diseases. Antioxidants neutralize free radicals by donating one of their own electrons, ending the electron-stealing reaction. Vitamin C does not become free radical by donating an electron because it is stable in either form. Vitamin C also has role in protecting other antioxidant vitamins (Vitamin A and Vitamin E) from the harmful effects of oxidation. All of biochemical and molecular functions of Vitamin C are because of its antioxidant effect.

Zinc – Anti-rhinoviral Effect

Zinc has been found to inhibit rhinovirus (virus usually causing common cold) replication in-vitro. Zinc produces interruption of viral binding sites. Further, zinc may coat the rhinoviruses and prevent them from attaching to the nasal cells. When zinc supplementation provided within 24 hours of cold symptoms begins, it reduces durations as well as severity of the cold symptoms. The zinc-treated patients also have significantly fewer days of coughing, headache, hoarseness, nasal congestion, nasal drainage and sore throat.

5.2Pharmacodynamic Properties

Ascorbic Acid

Vitamin C is needed for normal growth and development. Vitamin C plays important role in supporting a healthy immune system. Vitamin C deficiency impairs the immune defence reactions, especially chemotaxis, complement activation and interferon production.

Vitamin C has several important functions in the human body. These include:

- Protect cells and keep them healthy.

- Boosting of immune system (increases natural killer cell activities, lymphocyte proliferation, and chemotaxis; also stimulates leukocyte functions, especially of neutrophils and monocytes).
- Helping with wound healing and repair.
- Essential for the growth and repair of tissue all over the body.
- Maintaining healthy skin, blood vessels, bones, teeth, and cartilage.
- Improves absorption of iron (by forming a chelate with ferric iron at acid pH that remains soluble at the alkaline pH of the duodenum).
- Shorten the duration of cold symptoms and also reduces severity of symptoms.
- Reduces risk of chronic diseases.
- Protect against eye diseases.

Zinc

Zinc ions (Zn^{++}) at physiologic pH produces activities such as anti-rhinoviral effect, aids immune system, induces interferon, closes cell / plasma membrane pores, and possesses anti-inflammatory, antioxidant and protease inhibitors actions. Zinc deficiency has been reported to impair cellular mediators of innate immunity such as phagocytosis and natural killer cell activity.

5.3Pharmacokinetics Properties

Ascorbic Acid

Absorption: Ascorbic acid is absorbed in the proximal small intestine in a concentration-dependent manner. As the unit dose increases the absorption of ascorbic acid decreases. With 30-180 mg/day of vitamin C intake, there is 70 to 90% absorption, whereas, with intake greater than 1 g/day, the absorption drops to less than 50%. The unabsorbed proportion is broken down by the flora in the large intestine, predominantly to CO2 and organic acids.

Distribution: The total body content of ascorbic acid is about 1.5 g. Ascorbic acid accumulates in the pituitary gland, adrenal glands, lenses of the eyes and white blood cells. The body tightly regulates tissue and plasma concentrations of vitamin C, thus, toxicity is extremely rare.

Metabolism and Excretion: Vitamin C is metabolized in the liver and excreted by the kidneys (more than 80% as unchanged). Excess vitamin C is excreted unchanged in the urine. When plasma concentration of vitamin C is low, excretion of vitamin C decreases. The mean half-life is 2.9 hours. Renal excretion takes place by glomerular filtration followed by reabsorption in the proximal tubule.

Zinc

Absorption of zinc from the gastrointestinal tract is incomplete, and is reduced in the presence of some dietary constituents such as phytates. Bioavailability of dietary zinc varies widely between different sources, but is about 20 to 30%. Zinc is distributed throughout the body with the highest concentrations found in muscle, bone, skin, eye, and prostatic fluids. It is primarily excreted in the faeces, and regulation of faecal losses is important in zinc homoeostasis. Small amount of zinc is lost in urine and perspiration.

6. Nonclinical Properties

6.1 Animal Toxicology

Ascorbic Acid

Ascorbic acid has been shown to have very low acute oral toxicity in a range of species with values greater than 5 grams per kg being obtained in most cases. The compound has been shown to have very low toxicity on repeated exposure. Ascorbic acid was not toxic to rats in a 90-day study (oral gavage) at doses up to 5800 mg/kg body weight and day (male rats) and 4000 mg/kg body weight and day (female rats). Based on these results, the maximum dose level for the carcinogenicity studies was defined to be 50,000 ppm in the feed.

Zinc

The acute toxicity of zinc varied with the zinc salt used, and ranged from 237 to 623 mg/kg in rats and from 86 to 605 mg/kg in mice after oral administration; the acute toxicity following an intraperitoneal dose ranged from 28 to 73 mg/kg in rats and from 32 to 115 mg/kg in mice.

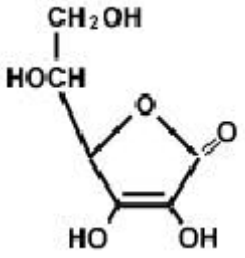
7. Description

BLUVIT-CZ Tablets are light orange coloured, slight mosaic appearance, circular flat, beveled edged, uncoated tablet plain on both sides.

BLUVIT-CZ Tablets contain Ascorbic Acid 100 mg, Sodium Ascorbate 450 mg, and Zinc Citrate 5 mg for oral administration in adults.

Ascorbic Acid

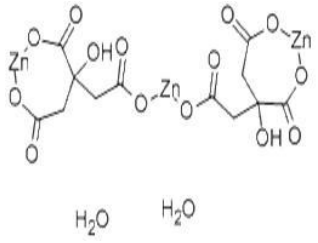
Ascorbic acid (vitamin C) is a water-soluble vitamin. It occurs as a white or slightly yellow crystal or powder with a slight acidic taste. On exposure to light, it gradually darkens. In the dry state, it is reasonably stable in air, but in solution it rapidly oxidizes. Ascorbic acid (vitamin c) is freely soluble in water; sparingly soluble in alcohol; insoluble in chloroform, in ether, and in benzene. The chemical name is L-ascorbic acid (vitamin C). The molecular formula is C6H806, and the molecular weight is 176.13. The structure is as follows:



Zinc Citrate

Zinc citrate is a colourless powder. Zinc Citrate contains the zinc salt form of citric acid for the purpose of providing zinc. As an essential trace element, zinc is of key importance in many biological processes.

Molecular Formula: C12H10O14Zn3
Molecular Weight: 574.3g/mol.
Structural formula is as follows:



Inactive ingredients (excipients) of BLUVIT-CZ Tablets contain Lactose, Colloidal Silicon Dioxide, Isomalt, Flavour Powderom Orange, Sucralose, Colour - Sunset Yellow, Magnesium Stearate, and Talcum.

8. Pharmaceutical Particulars

8.1 Incompatibilities

None known.

8.2 Shelf-life

18 months.

8.3 Packaging Information

15 tablets per strip.

8.4 Storage and Handling Instructions

Store protected from light and moisture, at a temperature not exceeding 25 °C.
Keep out of reach of children.

9. Patient Counseling Information

Administration Instructions

Instruct patients to:

- Take prescribed dose of BLUVIT-CZ Tablets as directed.
- Chew or crush tablets completely before swallowing.

10. Details of Manufacturer

Akums Drugs & Pharmaceuticals Ltd.
Plot No. 19, 20 & 21, Sector-6A, I.I.E., SIDCUL,
Ranipur, Haridwar – 249403, Uttarakhand.

11. Details of Permission or License Number with Date

DCG(I) NOC Date: 17/07/2015.
Mfg. Lic. No.: 5/UA/SC/P-2004.
Date of FDA Product Permission: 03/10/2020.

12. Date of Revision

March 2021.

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