For the use of a Registered Medical Practitioner only

1.GENERIC NAME & BRAND NAME

Ascorbic Acid (Vitamin C) and Zinc Chewable Tablets

LIMCEE® Zinc

2. QUANTITATIVE AND QUANTITATIVE COMPOSITION:

Each Uncoated Chewable Tablet Contains:
Ascorbic acid I.P.…….100 mg
Sodium Ascorbate I.P.....…450 mg
Eq. to Ascorbic Acid…..…400 mg
Zinc Citrate I.P. Eq. to Elemental Zinc……5 mg
Excipients……..q.s.
Colour: Lake of Sunset Yellow FCF

3.DOSAGE FORM AND STRENGTH

Kindly refer to section 1& 2

4.CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

For the prevention and treatment of Vitamin C & Zinc deficiency.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

The recommended adult dose is 1-2 tablets daily or as directed by the Physician.

Special population

Adults and Children ≥ 13 years: 1-2 tablets per day until symptoms abate.
Children 6-12 years: 1 tablet per day or should be taken as advised by the Physician.
Children under 6 years: This unit dosage form is unsuitable for children under 6 years. Hence, these formulations are not recommended for use in children under 6 years.
Elderly: As for other adults. As the dietary intake of vitamin C may be less in the elderly, they have greater risk of presenting with vitamin C deficiency.
Renal Impairment: Caution is required in patients with renal impairment.

The therapy duration depends on the physiological need (e.g., in case of increased physical strain) and on condition associated with vitamin C deficiency (e.g., burns, alcoholism or scurvy) and zinc deficiency. Vitamin C & Zinc combination tablets should be administered over the period of the physiological need or until the symptoms abate.

The maximum therapeutic dose of vitamin C should not be exceeded 1000 mg per day (1000mg/day).

Method of administration: For oral use only. The Vitamin C & Zinc chewable tablets are to be chewed before swallowing.

4.3 CONTRAINDICATIONS

Ascorbic acid (vitamin C) & zinc chewable tablets are contraindicated in:
• Hypersensitivity to any of the active substance(s) or any of the other constituents.
• Ascorbic acid should not be given to patients with hyperoxaluria.

• Oxalate urolithiasis and iron storage diseases (thalassaemia, haemochromatosis, and sideroblastic anaemia) or other medical conditions that predispose individuals to iron overload.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Ascorbic acid (Vitamin C)

Increased intake of ascorbic acid over a prolonged period may result in an increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly.

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.

Ascorbic acid has caused haemolytic anaemia in certain individuals with a deficiency of glucose-6-phosphate dehydrogenase. Caution is required and use the minimum recommended dose in patients with renal impairment. Patients known to be at risk of hyperoxaluria should not ingest ascorbic acid in doses greater than 1g daily as there may be increased urinary oxalate excretion. In case of the susceptibility to renal calculi, there is the risk of the formation of calcium oxalate calculi due to the intake of high doses of vitamin C. Patients with recurring formation of renal calculi are recommended not to exceed a daily vitamin-C-uptake of 100 to 200 mg.

For patients with extreme or terminal renal insufficiency (patients of dialysis), respectively, a daily vitamin-C-uptake of 50 to 100 mg of vitamin C should not be exceeded, because otherwise, there is the risk of hyperoxalataemia and crystallizations of oxalate in the kidneys.

High dose vitamin C therapy should be avoided in patients with underlying renal insufficiency or urinary oxalate should be monitored in patients. Nephrotoxic symptoms can occur in patients with renal failure and patients who concomitantly use medicinal products with negative effect on the renal function, e.g., iron overload due to enhanced iron reabsorption.
Interference with serological testing.

- Ascorbic acid may interfere with tests and assays for urinary glucose, giving false-negative results with methods utilising glucose oxidase with indicator (e.g., Labstix, Tes-Tape) and false-positive results with neocuproine methods.
- Estimation of uric acid by phosphotungstate or uricase with copper reduction and measurement of creatinine in non-deproteinised serum may also be affected.
- High doses of ascorbic acid may give false-negative readings in faecal occult blood tests.
- Patients with rare hereditary fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase deficiency should not take ascorbic acid.

Zinc

Accumulation of zinc may occur in cases of renal failure.
Drugs which may inhibit zinc absorption, such as penicillamine, sodium valproate and ethambutol, should not be administered with Zinc, unless the risks of discontinuation of the drug are judged to outweigh the benefit.
Patients receiving other single vitamins or multivitamin preparations, any other medication or those under medical care should consult a health care professional before taking this product.

4.5 DRUG INTERACTIONS

Ascorbic acid (Vitamin C)

Administration of ascorbic acid leads to increased absorption of iron from the gastrointestinal tract. This should be borne in mind in the case of iron replacement.
Concurrent administration of ascorbic acid with desferrioxamine enhances urinary iron excretion. Cases of cardiomyopathy and congestive heart failure have been reported in patients with idiopathic haemochromatosis and thalassaemias receiving desferrioxamine 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. Ascorbic acid should be used with caution in these patients and cardiac function monitored.

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.

Concomitant administration of acetylsalicylic acid (aspirin) 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.
Ascorbic acid increases the renal excretion of amphetamine. The plasma concentration of ascorbate is decreased by smoking and oral contraceptives.

Co-administration with amygdalin (a complementary medicine) can cause cyanide toxicity.
Ascorbic acid may interfere with biochemical determinations of creatinine, uric acid, and glucose in samples of blood and urine.
Cyclosporine: Vitamin C may reduce cyclosporine blood levels.
Warfarin: High doses of vitamin C may interfere with the effectiveness of warfarin.
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.

Zinc

Zinc forms complexes with certain substances (including tetracycline antibiotics (but not doxycycline), quinolone antibiotics, penicillamine) resulting in decreased absorption of both substances. In addition, zinc may also interfere with the absorption of cephalexin or ceftibuten. An interval of at least three hours should be allowed between administration of zinc and any of these medicines. 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.
Tetracyclines: Zinc may reduce the absorption of concurrently administered tetracyclines, also the absorption of zinc may be reduced by tetracyclines; when both are being given an interval of at least three hours should be allowed.
Quinolones: Zinc may reduce the absorption of quinolones; ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin and ofloxacin.
Penicillamine: The absorption of zinc may be reduced by penicillamine; also, the absorption of penicillamine may be reduced by zinc.
Copper: Zinc may inhibit the absorption of copper.
Calcium Salts: The absorption of zinc may be reduced by calcium salts.

Iron: The absorption of zinc may be reduced by oral iron; also, the absorption of oral iron may be reduced by zinc.
Trientine: The absorption of zinc may be reduced by trientine; also, the absorption of trientine may be reduced by zinc.

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Pregnancy

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. Pregnant women should exercise caution. Zinc crosses the placenta.
The product should only be used in pregnancy when clinically indicated and recommended by a doctor or healthcare professional.

Lactation

The vitamin and mineral are excreted into the breast milk; this should be taken into consideration, especially if the infant is receiving any other supplements.
Ascorbic acid is excreted in breast milk. Though again caution should be exercised, no evidence exists suggesting such excretion is hazardous to the infant. Zinc crosses the placenta and is present in breast milk. Vitamin C and Zinc, both are secreted into breast milk. This must be taken into consideration if the infant is receiving any other supplements.

Paediatric population

This unit dosage form is unsuitable for children under 6 years. Hence, these formulations are not recommended for use in children under 6 years.

Renal Impairment

Caution is required in patients with renal impairment.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

On the basis of the product's pharmacodynamic profile and reported adverse events, ascorbic acid has no known effect on an individual's ability to drive or operate machinery.
Zinc has no influence on the ability to drive and use machines.

4.8 UDESIRABLE EFFECTS

Ascorbic acid (Vitamin C)

Adverse reactions reported from post-marketing experience are tabulated below by System Organ Class and frequency. The following convention has been utilized for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from available data).

Immune system disorders: Very rare: Allergic reactions, including hypersensitivity reactions (such as shortness of breath, swelling of the face and skin rash).
Nervous system disorders: Very rare: Headache and dizziness.
Gastrointestinal disorders: Very rare: Nausea, vomiting, diarrhoea, dyspepsia, and abdominal pain.

General disorders and administration site conditions: Very rare: Fatigue.

Side effects include nausea, vomiting, abdominal cramping, and headaches. Large doses of ascorbic acid may cause diarrhoea and the formation of renal calcium calculi.
Vascular disorders: flushing.
Skin and subcutaneous tissue disorders: redness of skin.
Renal and urinary disorders: Patients known to be at risk of hyperoxaluria should not ingest ascorbic acid doses exceeding 1g daily as there may be increased urinary oxalate excretion.

However, such risk has not been demonstrated in normal, non-hyper oxaluric individuals. Ascorbic acid has been implicated in precipitating haemolytic anaemia in certain individual's deficient of glucose-6-phosphate dehydrogenase.

Increased intake of ascorbic acid over a prolonged period may result in increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly. Doses of more than 600mg daily have a diuretic effect.

Zinc
Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	**Adverse drug reactions**
Blood and lymphatic system disorders	***uncommon:*** **sideroblastic anaemia, leukopenia**
Gastrointestinal disorders	***common:*** **gastric irritation**
Investigations	***common:*** **blood amylase, lipase and alkaline phosphatase increased**

Anaemia may be micro-, normo- or macrocytic and is often associated with leukopenia. Bone marrow examination usually reveals characteristic "ringed sideroblasts" (i.e. developing red blood cells containing iron-engorged paranuclear mitochondria). They may be early manifestations of copper deficiency and may recover rapidly following reduction of zinc dosage. However, they must be distinguished from haemolytic anaemia which commonly occurs where there is elevated serum free copper in uncontrolled Wilson's disease.
The most common undesirable effect is gastric irritation. This is usually worst with the first morning dose and disappears after the first days of treatment.
Delaying the first dose to mid-morning or taking the dose with a little protein may usually relieve the symptoms.
Elevations of serum alkaline phosphatase, amylase and lipase may occur after a few weeks of treatment, with levels usually returning to high normal within the first one or two years of treatment**.**

Zinc salts may cause abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, gastric irritation, and gastritis. There have also been cases of irritability, headache and lethargy observed.
Zinc may interfere with the absorption of copper, leading to reduced copper levels, and potentially copper deficiency. The risk of copper deficiency may be greater with long-term treatment (e.g., if zinc deficiency is no longer present) and/or with higher doses of zinc.

Vitamin C and Zinc combination
The combo of vitamin c and zinc 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.

4.9 OVERDOSE

There is no evidence that this product can lead to an overdose when used as recommended.
General manifestations of overdose with vitamin C and/or zinc may include increase of gastrointestinal disturbances including diarrhoea, nausea, and vomiting. If such symptoms occur, the product should be stopped, and a healthcare professional consulted.

Ascorbic acid (Vitamin C)

Symptoms: At doses of over 3g per day unabsorbed ascorbic acid is mainly excreted unmetabolized in the faeces. Absorbed ascorbic acid additional to the body's needs is rapidly eliminated. Large doses of ascorbic acid may cause diarrhoea and the formation of renal oxalate calculi. Symptomatic treatment may be required.

Ascorbic acid may cause acidosis or haemolytic anaemia in certain individuals with a deficiency of glucose 6-phosphate dehydrogenase. Renal failure can occur with massive ascorbic acid overdosage.

Management: Gastric lavage may be given if ingestion is recent otherwise general supportive measure should be employed as required. Vitamin C is removed by haemodialysis.

Zinc

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

Symptoms: High doses of zinc cause emesis. In addition, zinc sulfate is corrosive at high doses and may cause irritation and corrosion of the gastrointestinal tract, including ulceration of the stomach and possible perforation. Overdosage with zinc has also been associated with acute renal tubular necrosis and interstitial nephritis. Prolonged high dose zinc supplementation may result in copper deficiency.

Treatment: In cases of acute zinc overdose, treatment is primarily supportive; however induced emesis, gastric lavage, or activated charcoal may be useful in cases of substantial ingestions of zinc tablets. Chelating agents such as calcium disodium EDTA may be useful.
If overdose with the product is suspected, intake should be stopped and a health care professional consulted for treatment of clinical manifestations.

5.0 PHARMACOLOGICAL PROPERTIES

5.1 MECHANISM OF ACTION

Ascorbic acid (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. Further, a deficiency of vitamin C affects the immune defense reactions, particularly

chemotaxis, complement activation and interferon production. The molecular biological functions of vitamin C have not yet been fully explained.

Zinc
Zinc is an essential trace element which is present in a wide range of foods. It is found in all tissues. Normal growth and tissue repair depend upon adequate zinc levels. Zinc acts as an integral part of several enzymes important to protein and carbohydrate metabolism. Severe zinc deficiency is associated with growth retardation, primary hypogonadism, skin disease, disturbances of taste and smell, and impaired immunity, with increased susceptibility to infection. The beneficial effects of zinc are likely associated with reconstitution of the immune response, however direct inhibitory effects of zinc on enteric pathogens have also been reported.

5.2 PHARMACODYNAMIC PROPERTIES

Ascorbic acid (Vitamin C)
Ascorbic acid, coupled with dehydroascorbic acid to which it is reversibly oxidized, has a variety of functions in cellular oxidation processes. Ascorbic acid is required in several important hydroxylations, including the conversion of proline to hydroxyproline (and thus collagen formation e.g., for intercellular substances and during wound healing); the formation of the neurotransmitters 5-hydroxytryptamine from tryptophan and noradrenaline from dopamine, and the biosynthesis of carnitine from lysine and methionine. Ascorbic acid appears to have an important role in metal ion metabolism, including the gastrointestinal absorption of iron and its transport between plasma and storage organs. There is evidence that ascorbic acid is required for normal leucocyte functions and that it participates in the detoxification of numerous foreign substances by the hepatic microsomal system. Deficiency of ascorbic acid leads to scurvy, which may be manifested by weakness, fatigue, dyspnoea, aching bones, perifollicular hyperkeratosis, petechia and ecchymosis, swelling and bleeding of the gums, hypochromic anaemia, and other haematopoietic disorders, together with reduced resistance to infections and impaired wound healing.

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.

5.3 PHARMACOKINETIC PROPERTIES

Absorption
Ascorbic acid is absorbed in the proximal small intestine in a concentration-dependent manner. As the unit dose increases the bioavailability falls to 60-75% after 1 g, to approximately 40% after 3 g and down to 16% after 12 g. The unabsorbed proportion is broken down by the flora in the large intestine, predominantly to CO_2 and organic acids.
Zinc is absorbed all along the small intestine. The absorption of zinc (ionic) administered in solution on an empty stomach range 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. In healthy adults the maximum metabolic turnover of 40 to 50 mg/day is achieved at plasma concentrations of 0.8 to 1.0 mg/dl. The total daily turnover is about 1 mg/kg. At extremely high oral doses plasma concentrations of up to 4.2 mg/dl are achieved for a short time after about 3 hours.

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.

Excretion
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.
Ascorbic acid is excreted in the urine more than 80% unchanged. The mean half-life is 2.9 hours. Renal excretion takes place by glomerular filtration followed by reabsorption in the proximal tubule. Upper limit concentrations in healthy adults are 1.34 ± 0.21 mg ascorbic acid/dl in men and 1.46 ± 0.22 mg ascorbic acid/dl plasma in women. The total body content of ascorbic acid after high intake of about 180 mg a day is at least 1.5 g. Ascorbic acid accumulates in the pituitary gland, adrenal glands, lenses of the eyes and white blood cells.

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.

6.NONCLINICAL PROPERTIES
6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY
Not Available

7.0 DESCRIPTION
Light Orange coloured, slight mosaic appearance, circular, flat, beveled edged, uncoated tablets, plain on both sides. 15 tablets packed in a strip of printed aluminium foil & plain aluminium foil.

8.0 PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES
Not Applicable

8.2 SHELF-LIFE
Refer Pack

8.3 PACKAGING INFORMATION
Refer Pack

8.4 STORAGE AND HANDLING INSTRUCTIONS
Refer Pack

9. PATIENT COUNSELLING INFORMATION
Ascorbic Acid Tablets contain ascorbic acid. Ascorbic acid is a form of vitamin C. It is used as a supplement for the prevention and treatment of scurvy. Do not take Ascorbic Acid Tablets if: You are allergic to Ascorbic Acid or any of the other ingredients of this medicine. You suffer from hyperoxaluria (excretion of urine containing large amounts of calcium oxalate crystals). Talk to your doctor or pharmacist before taking Ascorbic Acid Tablets: If you are to undergo any blood or urine tests as ascorbic acid can interfere with some blood and urine tests. If you have kidney failure as ascorbic acid enhances aluminium absorption (present in antacids) which may reach toxic levels. Stop taking this medicine immediately and consult your doctor if you suffer an allergic reaction after taking this medicine. An allergic reaction may include itching, a rash, swelling of the face, lips, tongue, and/or throat with difficulty in swallowing or breathing.

10. DETAILS OF MANUFACTURER
Refer pack for manufacturer details.

Marketed By:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. No. D-4,
Gala No. 1 to 3 & 11 to 13 Ground Floor,
101 to 106 & 111 to 116 First Floor,
201 to 206 & 211 to 216 2nd Floor,
Pimplas, Dist. Thane,
Bhiwandi-421 302, Maharashtra, India.

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11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE
5/UA/SC/P-2004, dated 24-Feb-25

12. DATE OF REVISION
Version: 1.0, Dated: 19-Mar-25

For Product Complaints/Adverse events or Queries please write to
webmasterindia@abbott.com