APPROVED
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INSTRUCTION
For medical use

ASCOZIN®

Composition:
active substances: ascorbic acid, sodium ascorbate, zinc oxide;
1 tablet contains ascorbic acid 100 mg, sodium ascorbat that is equivalent to ascorbic acid 400 mg, zinc oxide that is equivalent to zinc 15 mg;
excipients: manitol (E 421), povidone K30, crosspovidone, sunset yellow FCF (E 110), ethylcellulose, aspartam (E 951), magnesium stearate, orange flavor 844763.

Pharmaceutical form. Chewable tablets.
Main physical and chemical properties: round biconvex light-orange tablets with speckles.

Pharmacotherapeutic group.
Drugs of ascorbic acid (Vitamin C), combinations.
Code ATC A11G B.

Pharmacological properties.
Pharmacodynamics.
Ascozin® is a coformulated drug consisting of two drug substances: a water-soluble vitamin C - ascorbic acid and micronutrient - zinc.
Ascorbic acid mode of action.
As antioxidant, metabolic, and redox processes regulating agent ascorbic acid (vitamin C) increases adaptive capacity of organism, enhances its resistance to infections. It maintains colloidal condition of intercellular substance and normal capillary penetration (it inhibits hyaluronidase). It participates in regulation of redox processes, in carbohydrate metabolism, aromatic amino acid, pigments and cholesterine, in synthesis of steroid hormones, catecholamines, and in blood coagulation. It enhances collagen synthesis, stimulates regeneration processes, and normalizes capillary penetration. Due to activation of respiratory ferments in liver it enhances its detoxification and protein generating function, enhances synthesis of collagen and prothrombin. It improves bile excretion, renews exocrinous function of pancreas. It inhibits excretion and accelerates histamine degradation, inhibits formation of prostaglandins and other inflammation and anaphylactic mediators. It regulates immunological reactions (activates synthesis of antibodies, C_3-component of the complement system, interferon), facilitates phagocytosis, elevates organism resistance to infections. It has an anti-inflammatory and anti-allergic action.
Zinc mode of action
Zink is a structural component of biological membranes, cell receptors, proteins; it is a component of more than 200 enzyme systems. It takes part in reactions of immune and anti-oxidant protection, blood formation, amino acids synthesis, in genetic information preservation and transmission. Being a component of protein, which transmits retinol, zinc together with vitamin A and vitamin C prevents immune deficit formation, stimulating antibody synthesis and causing antiviral action.
Zinc promotes growth and development of cells, the correct functioning of the immune system and provides immune response, twilight vision, taste and smell perception. It affects the preservation of normal blood levels of vitamin A, prolongs time of action of insulin and facilitates its accumulation. In inflammatory skin condition has preventive and therapeutic actions.

Zinc deficiency causes difficulties in concentration and memory, poor appetite and distorted taste, decreased cellular and humoral immunity, poor wound healing, night blindness, carbohydrate balance disorders, hypercholesterolemia, hypertension, mental and brain disorders, prostate hypertrophy, violation of pregnancy, hypogonadism and growth suppression in children and, to a large extent, dermatological disorders (senile alopecia, alopecia areata, acne). In high doses, zinc inhibits copper absorption. Zinc deficiency also increases the absorption of toxic cadmium.

Pharmacokinetics.

For ascorbic acid.

Absorption. Ascorbic acid is absorbed mainly in the upper part of the small intestine through sodium-dependent active transport. If ascorbic acid is present at high concentrations, then its absorption also occurs via passive diffusion. With the increasing of ascorbic acid oral doses from 1 g to 12 g, the drug absorption specific weight was decreased (approximately 50% to 15%). The gastrointestinal tract disorders (gastritis, ulcer, constipation, diarrhea, helminthosis, giardiasis), the intake of fresh fruit and vegetable juice and alkaline drinking may disturb the absorption of vitamin C.

Distribution: The binding of ascorbic acid to blood plasma proteins is approximately 24%. As a rule, the ascorbic acid blood serum concentration is 10 mg/L (60 μmoll/L) in terms of adequate ascorbic acid intake. The reduction of ascorbic acid blood serum concentration below 4 mg/l (20 μmoll/L) indicates poor intake of vitamin C.

Metabolism: Ascorbic acid is metabolised partly via dehydroascorbic acid to oxalic acid and other products. When ingested in excessive quantities, ascorbic acid is largely excreted in unchanged form in the urine and faeces. Ascorbic-acid-2-sulphate also appears as ascorbic acid metabolite in the urine. Smoking and ethyl alcohol abuse accelerates ascorbic acid decay (transformation into inactive metabolites), sharply decreasing its reserve in organism. The physiological level of ascorbic acid depot in organism is about 1.5 g. It deposes in the back of the pituitary, adrenal cortex, epithelium of the eye, intermediate cells of seminal glands, ovaries, liver, brain, spleen, pancreas, lungs, kidneys, intestine wall, heart, muscle, thyroid gland. It easily penetrates from plasma into leucocytes, platelets, and almost all tissues.

Elimination: Unchanged ascorbate and its metabolites are excreted by the kidneys, intestine, through sweat and penetrate into breast milk. The half-life of ascorbic acid depends on the route of administration, the quantity administered and the rate of absorption. Following an ascorbic acid oral dose of 1 g the half-life is about 13 hours. When up to 3 g ascorbic acid/day is taken, the main route of excretion is renal. With doses exceeding 3 g/day, it is excreted both in the faeces and urine (unchanged).

For zinc.

Absorption: Zinc is absorbed along the entire small intestine. If taking zinc under fasting condition and as aqueous solution, the drug absorption will be up to 41-79%. If taking zinc with food, the drug absorption is 10-40%.

Distribution and metabolism: The maximum plasma zinc concentration is observed within 2 hours after ingestion. In the body, zinc accumulates predominantly in leukocytes and erythrocytes, as well as in muscles, bones, skin, kidneys, liver, pancreas and prostate, retina. Zinc binding is 60% to albumin, 30 - 40% to alpha-2 macroglobulins, 1% to amino acids, predominantly like histidine and cysteine.

Elimination: Zinc is excreted from the body mainly in the feces (90%) and to a lesser extent in urine and sweat. Calcium supplements and calcium rich diet (dairy products) may reduce zinc absorption by 50%, but caffeine and alcohol intensely eliminate it from the body.

Clinical characteristics.

Indications.

As a component of combination treatment of conditions and diseases caused or accompanied by zinc deficiency and ascorbic acid hypovitaminosis:

- susceptibility to catarrhal and infectious diseases;
- diseases associated with decreased immunity;
- bleedings (uterine, pulmonary, nasal, in radiation sickness), overdose of anticoagulants, increased permeability and fragility of blood vessels;
- liver disease (hepatitis A, chronic hepatitis, cirrhosis);
- nephropathy of pregnancy;
- dystrophy, broken bones and wounds that do not heal for a long time;
- destruction of connective tissue (rheumatoid arthritis, systemic lupus erythematosus, scleroderma);

- disorders of carbohydrate and fat metabolism;
- dysfunction of the endocrine glands, Addison's disease;
- hypofunction of the prostate;
- atherosclerosis;
- bronchial asthma.

Contraindications.

- Hypersensitivity to any component of the drug.
- Liability to thrombosis, thrombophlebitis.
- Diabetes mellitus.
- Urinary stone disease, severe kidney diseases, severe renal failure.
- Phenylketonuria.
- Special caution should be exercised when prescribing in patients with violation of iron metabolism (hemosiderosis, hemochromatosis, thalassemia).

Special precautions.

Associated with ascorbic acid.

Since vitamin C has a slight stimulating effect, it is not recommended to take it at the end of the day.

Since ascorbic acid has stimulating effect on corticosteroid hormones formation, when using it in high doses, it is necessary to control kidney function and blood pressure.

The drug should be used with caution in case of hypercoagulability.

Special caution should be exercised when prescribing in patients with:

- glucose-6-phosphate dehydrogenase deficiency (high doses of ascorbic acid may provoke hemolytic anemia);
- with the history of nephrolithiasis (there is a risk of hyperoxaluria and oxalate residues in the urinary tract after the intake of high doses of ascorbic acid).

Long-term administration of high doses of ascorbic acid may increase its own metabolism, which may lead to paradoxical hypovitaminosis after discontinuation of treatment. Do not exceed the recommended dose.

Do not use simultaneously with other drugs containing vitamin C.

Caution should be exercised when using the drug in patients with polycythemia, leukemia.

The absorption of ascorbic acid may be impaired in case of intestinal dysmotility, enteritis or acrylic (reduced gastric secretion).

It should be taken into account that using high doses of vitamin C may alter some laboratory parameters (blood glucose, bilirubin, transaminases, uric acid, creatinine, inorganic phosphates). The fecal occult blood test may be negative.

Associated with zinc.

During the use of zinc-containing drugs, the risk of copper deficiency should be taken into account. Diet rich in fibrin (e.g. bran), phosphates (e.g. milk products), whole-wheat bakery products and phytinates decreases zinc absorption due to the formation of complexes. The break between eating the above products and using the zinc-containing drugs should be not less than 2 hours.

Interaction with other medicinal products and other forms of interactions.

Interactions associated with ascorbic acid.

When applied simultaneously, ascorbic acid increases the absorption of iron, penicillin, ethinylestradiol in the gastrointestinal tract. Similar effect applies to aluminium, therefore it should be considered by simultaneous treatment with antacids that contain aluminium.

Ascorbic acid decreases the effectiveness of heparin and anticoagulants when applied simultaneously.

The absorption of ascorbic acid is decreased when applied simultaneously with oral contraceptives, fruit or vegetable juices, alkaline drinks. Simultaneous application of vitamin C and deferoxamine increases the tissue toxicity of iron, especially in the cardiac muscle that may lead to circulatory decompensation. Vitamin C should be taken only 2 hours after deferoxamine injection. Long-term use of large doses of ascorbic acid reduces the efficiency of treatment with disulfiram.

Large doses of the product decrease the efficiency of tricyclic antidepressants, antipsychotics – derivatives of phenothiazine, tubular reabsorption of amphetamine, violate excretion of mexiletine by kidneys.
Ascorbic acid increases the total clearance of ethyl alcohol. Such quinolone drugs as calcium chloride, salicylate, tetracyclines, corticosteroids with long-term use reduce supplies of ascorbic acid in body.
At high doses, ascorbic acid affects resorption of vitamin B_{12}.
Vitamin C increases urinary oxalate excretion and thus enhances the risk of oxalate stone formation in the urine. Vitamin C increases the risk of crystalluria in the treatment of salicylates.
Interactions associated with zinc.
Tetracyclines. Zinc decreases absorption of tetracyclines and blocks absorption of copper (in case of using high doses of zinc), thus the drug should be taken not earlier than 2 hours after the drugs application.
Copper products. High doses of copper can inhibit copper absorption (zinc salts should be used not earlier than 2 hours after the drugs application).
Thiazide diuretics increase urinary excretion of zinc.
Diet rich in fibrin (e.g., siftings), phosphates (e.g., dairy products), whole grain breadstuffs and phitinates decreases absorption of zinc due to complex formation, hence a break between the usage of above mentioned products and of zinc products should be not less than 2 hours.
Folic acid violates the absorption of zinc only inconspicuously.
When taken orally, high doses of *iron* decreases significantly the absorption of zinc (the drug should be taken not earlier than 2 hours after taking these drugs).
Penicillamine and other chelating agents reduce the absorption of zinc (the drug should be taken not earlier than 2 hours after taking these drugs).
Using the drug Ascozin® together with *multivitamin and mineral supplements*, which include zinc, remember about the possibility of overdose.
Quinolones. Zinc reduces the absorption of antibiotics containing quinolones and of fluoroquinolones.

Administration details.
The drug contains: colorant yellow sunset FCF (E110), which may cause allergic reactions; aspartame (E 951), a derivative of phenyl alanine, that represents a danger for patients with phenylketonuria.

Use in pregnancy and lactation.
Pregnancy.
Neither controlled studies during pregnancy nor controlled studies on animals have been conducted therefore the drug should be used only if, to the doctor`s opinion, the benefit for the mother outweighs the potential risk for the fetus.
Lactation.
Ascorbic acid and zinc penetrate into the breast milk. Therefore, while breastfeeding, the drug should be used under the supervision of a doctor.

Influence on velocity reactions in driving motor transport or operating other machines.
There is no indication that the drug can adversely affect drivers or people who work with complex machinery.

Administration and dosage.
Ascozin® should be taken orally after meal; the tablet should be chewed and washed down with a little amount of water. Duration of treatment depends on the nature and the course of a disease.
Adults should take one tablet once a day.
Duration of treatment is determined by the physician depending on the nature and the course of a disease.
By pronounced hypovitaminosis and treatment of infectious diseases, adults should take one tablet twice a day for 5-7 days.

Children.
Ascozin® is contraindicated for children.

Overdose.
There is no evidence that this product can lead to an overdose when used as recommended.

Allowance should be made for intake of vitamin C and zinc from all other sources.
Clinical signs and symptoms, laboratory findings, and consequences of overdose are highly diverse, dependent on an individual susceptibility and surrounding circumstances.
General manifestations of overdose with vitamin C and/or zinc may include increase of gastrointestinal disturbances including diarrhea, nausea, and vomiting.
If such symptoms occur stop drug administration and consult your physician.
Specific clinical manifestations may include the following:
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 doctor before use of the product.
Overdose of vitamin C may result in oxidative hemolysis or disseminated intravascular coagulation in patients with glucose-6-phosphate dehydrogenase deficiency.
Zinc.
Zinc overdose can cause irritation and corrosion of mucosa of the gastrointestinal tract, acute tubular necrosis, interstitial nephritis, copper deficiency, sideroblastic anemia, and myeloneuropathies.
If overdose with the drug is suspected, intake should be stopped and a physician consulted for treatment of clinical manifestations. Vitamin C is removed by hemodialysis.

Adverse reactions.
Gastrointestinal disorders: irritation of mucosa of the gastrointestinal tract, dyspepsia, nausea, vomiting, pyrosis, stomachache, abdominal discomfort, diarrhea, gastritis, metallic aftertaste.
Immune system disorders: allergic reactions, including anaphylactic reactions, anaphylactic shock, hypersensitivity reactions including asthmatic syndrome, bronchospasm, cardiorespiratory distress, skin rashes, itching, eczema, hives, angioedema.
Nervous system disorders: hyperexcitability, increased fatigue, sleep disorders, headache.
Renal and urinary system disorders: damage of kidney glomeruli, renal insufficiency, crystalluria, formation of urate, cystine and oxalate calculuses in kidneys and urethra.
Skin and hypoderm disorders: rashes, itching.
Blood system disorders: thrombocytosis, thrombosis, hemolytic anemia, hyperprothrombinemia, erythropenia, heterophilic leukocyte; in patients with insufficiency of glucose-6-phosphate dehydrogenase blood corpuscles may cause erythrocyte hemolysis; hematologic disorders caused by copper deficiency, including leukopenia (fever, chills, sore throat), neutropenia (ulcers in the mouth and throat), sideroblastosis anemia (fatigue, weakness);
Endocrine system disorders: damages in the insular apparatus of the pancreas (hyperglycemia, glycosuria) and violation of glycogen synthesis till the appearance of diabetes.
Cardiovascular system disorders: arterial hypertension, myocarditis.
Metabolic disorders: metabolic imbalance of zinc, copper.
Others: fever sensation.

Shelf- life. 3 years.

Storage conditions.
Store at a temperature NMT 25 °C.
Keep out of reach of children**.**

Package.
10 tablets are in a strip, 3 or 10 strips are in a carton pack.

Conditions of supply.
Without prescription.

Manufacturer.

KUSUM HEALTHCARE PVT LTD.

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SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

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