

Summary of Product Characteristics

1. Name of the medicinal product

C-ZAD 100 mg ascorbic acid tablets

2. Qualitative and quantitative composition

Each tablet contains 100mg ascorbic acid

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablets.

4. Clinical particulars

4.1 Therapeutic indications

Vitamin C deficiency

Treatment and prevention of scurvy

4.2 Posology and method of administration

Posology

Adults:

Therapeutic use – at least 250mg daily in divided doses.

Prophylactic use – 25-75mg daily.

Maximum of 1000mg daily.

Paediatric population: (4-12 years): Half the adult dose (at least 125mg daily in divided doses).

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.

Method of Administration

For oral administration

4.3 Contraindications

Ascorbic acid should not be given to patients with hyperoxaluria.

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

4.4 Special warnings and precautions for use

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period may result in increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly. (See section 4.8)

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, Testape) and false-positive results with neocuproin 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.

4.5 Interaction with other medicinal products and other forms of interaction

Ascorbic acid increases the renal excretion of amphetamine. The plasma concentration of ascorbate is decreased by smoking and oral contraceptives.

Ascorbic acid increases the absorption of iron.

Concomitant administration of 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.

Concomitant administration of aluminium-containing antacids may increase urinary aluminium elimination. Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.

Co-administration with amygdalin (a complementary medicine) can cause cyanide toxicity.

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. Ascorbic acid should be used with caution in these patients and cardiac function monitored.

Ascorbic acid may interfere with biochemical determinations of creatinine, uric acid and glucose in samples of blood and urine.

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

Ascorbic acid is excreted in breast milk. Though again caution should be exercised, no evidence exists suggesting such excretion is hazardous to the infant.

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.

4.8 Undesirable effects

Nervous system disorders: headache.

Vascular disorders: flushing

Gastrointestinal disturbances: nausea, vomiting and stomach cramps.

Large doses of ascorbic acid may cause diarrhoea.

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.

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.

Ascorbic acid has been implicated in precipitating haemolytic anaemia in certain individuals deficient of glucose-6-phosphate dehydrogenase.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Symptoms

At doses of over 3gm per day unabsorbed ascorbic acid is mainly excreted unmetabolised 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 dyhydrogenase. Renal failure can occur with massive ascorbic acid overdosage.

Management

Gastric lavage may be given if ingestion is recent otherwise general supportive measures should be employed as required

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC Code of Ascorbic Acid : A11GA01

Ascorbic acid, coupled with dehydroascorbic acid to which it is reversibly oxidised, 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 in 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 hyperkeratoses, 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.

5.2 Pharmacokinetic properties

Ascorbic acid is well absorbed from the gastro-intestinal tract, and is widely distributed to all tissues. Body stores of ascorbic acid normally are about 1.5g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma. Ascorbic acid additional to the body's needs, generally amounts above 200mg daily, is rapidly eliminated; unmetabolised ascorbic acid and its inactive metabolic products are chiefly excreted in the urine. The amount of ascorbic acid excreted unchanged in the urine is dose-dependent and may be accompanied by mild diuresis.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the SmPC.

6. Pharmaceutical particulars

6.1 List of excipients

- lactose monohydrate,
- L- hydroxypropylcellulose

- magnesium stearate

6.2 Incompatibilities

None known

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Keep the container tightly closed. Store in the original container.

6.5 Nature and contents of container

Carton box with 250 tablets (25 blisters x 10 tablets) of 500 mg ascorbic acid.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

ZADA Pharmaceuticals Ltd.

Donji Bistarac without number

75 300 Lukavac

Bosnia and Herzegovina

8. Marketing authorisation number(s)

04-07.3-2-6379/15

9. Date of first authorisation/renewal of the authorisation

20.03.2017.

10. Date of revision of the text

16 August 2018