SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ASCORVİT 500 mg/5 mL solution for injection
Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient:
Each ampoule (5 mL) contains 500 mg vitamin C (ascorbic acid).

Excipients:

Methyl paraben (E218)	4 mg
Propyl paraben (E216)	0.5 mg
EDTA disodium	2.5 mg
Sodium Hydroxide	q.s. (pH adjuster)

For the full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Sterile and clear, colorless to yellow, particle-free solution in a clear glass ampoule.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- In severe vitamin C deficiency,
- It is used to eliminate or prevent vitamin C deficiency in cases where oral use is insufficient, not possible or contraindicated.

4.2. Posology and method of administration

Posology/frequency and duration of administration:
Dosage for adults:
In severe vitamin C deficiency, it is used at a dose of 500-1000 mg/day for up to 10 days.

It is used at a dose of 200-500 mg/day to eliminate or prevent vitamin C deficiency in cases where oral use is insufficient, not possible or contraindicated.

Dosage for children:
For the treatment of severe vitamin C deficiency, it is used at a dose of 100-300 mg/day, 1-2 times a day for 2 weeks-3 months, depending on the improvement of the symptoms.
Parenteral vitamin C is used at 15-25 mg/kg/day for preterm babies who are parenterally fed and for whom oral intake is not possible, and for children aged 0-12 months, and for children aged 1-18 years, 80 mg/day parenteral vitamin C is used.

Elderly:
No specific dosage requirements are suggested.

Route of administration:
It is given intramuscularly or intravenously. Intramuscular administration is preferred. When administered intravenously, it should be administered by slow infusion. Rapid intravenous injection may cause temporary drowsiness.

Additional information on special populations
Renal failure:
It should be used with caution.

Hepatic failure:
No specific dosage recommendation is given.

Pediatric population:
For the treatment of severe vitamin C deficiency, it is used at a dose of 100-300 mg/day, 1-2 times a day for 2 weeks-3 months, depending on the improvement of the symptoms.

Parenteral vitamin C is used at 15-25 mg/kg/day for preterm babies who are parenterally fed and for whom oral intake is not possible, and for children aged 0-12 months, and for children aged 1-18 years, 80 mg/day parenteral vitamin C is used.

Geriatric population:
There are no special dosage recommendations for the elderly.

4.3. Contraindications

- It should not be used in people known to have hypersensitivity reactions to ascorbic acid or any of its ingredients.
- It should not be used in hyperoxaluria.

4.4. Special warnings and precautions for use

- Acute and chronic vitamin C intake from all sources increases the risk of adverse effects when >1200 mg/day in children aged 9-13 years, >1800 mg/day in young adults aged 14-18 years, and >2000 mg in adults.
- Those with renal impairment may be sensitive to the toxic effects of vitamin C at low doses and the product should be used with caution.
- Because vitamin C increases iron absorption, high doses may be dangerous in patients with thalassemia, polycythemia, leukemia, or sideroblastic anemia. In case of iron overload disease, ascorbic acid intake should be kept to a minimum.

- It has been demonstrated that high doses of ascorbic acid are associated with sickle cell crises in sickle cell anemia patients.
- Chronic use of high doses of ascorbic acid may lead to increased metabolism of the drug. Therefore, withdrawal symptoms may occur when the dosage is reduced suddenly. In such a case, the high dosage should be returned and the dosage should be reduced more slowly.
- When high-potency vitamins are infused too quickly, pain and rarely thrombophlebitis may develop along the vein due to chemical irritation. Therefore, the solution should be infused slowly and care should be taken to avoid extravasation during the infusion. As is true for all parenteral solutions, care should be taken not to overload the circulatory system, especially in heart and lung patients.
- The diabetogenic effect of ascorbic acid is still controversial. However, blood glucose concentration in patients receiving long-term ASCORVİT treatment should be monitored periodically, especially during the initial period of treatment.
- Theoretically, high doses of ascorbic acid may cause gouty arthritis in susceptible patients due to its effect on uric acid excretion.
- It is thought that ascorbic acid may aggravate rapidly proliferating and widely spread tumors. Therefore, caution should be exercised when prescribing ascorbic acid in advanced cancers.
- Patients taking other single vitamin or multivitamin preparations, other medications, or under medical care should consult a healthcare professional before taking this product (see sections 4.5 and 4.9).

Oxalate nephropathy, nephrolithiasis and renal failure

Prolonged use of high doses of vitamin C may lead to oxalate nephropathy. The risk of developing oxalate stones is increased when using vitamin C in patients with renal failure, nephrolithiasis, the elderly and children under 2 years of age. Vitamin C treatment should be discontinued in patients who develop oxalate stones. Renal function should be monitored in all patients receiving vitamin C therapy.

G6PD Deficiency

High doses of vitamin C should be used with caution in patients with G6PD deficiency as it may cause hemolysis.

Hemachromatosis

Desferoxamine should be used with caution as it may increase its side effects and toxicity.

Laboratory Test Interference

It may lead to false positive and negative results in glucose measurements using glucose oxidase and copper sulfate, nitrite and bilirubin determinations and leukocyte count.

This medicinal product contains 72.24 mg sodium in each 5 mL dose. This should be taken into consideration for patients on a controlled sodium diet.

ASCORVİT may cause allergic reactions (possibly delayed) and exceptionally bronchospasm due to its content of methyl paraben (E218) and propyl paraben (E216).

4.5. Interaction with other medicinal products and other forms of interaction

Various potential interactions are reported in the literature for individual components. Therefore, patients taking any other medications, dietary supplements, or undergoing medical treatment should consult a physician or healthcare professional before taking this product.

Drug interactions

Warfarin: High doses of ascorbic acid may inhibit the effectiveness of warfarin.

Dicoumarol: There is an exceptional case in which prothrombin time was shortened after ingestion of ascorbic acid.

Disulfiram: Chronic or high doses of ascorbic acid may inhibit the effectiveness of disufram.

Desferrioxamine: Ascorbic acid may increase tissue iron toxicity, especially in the heart, leading to cardiac failure

Cyclosporine: Antioxidant supplementation, including vitamin C, may reduce blood levels of cyclosporine.

Indinavir (protease inhibitors): High doses of vitamin C may inhibit the effectiveness of indinavir, as it significantly reduces the serum concentration of indinavir.

Ethinylestradiol: Ascorbic acid at a dosage of 1 gram per day increases the bioavailability of ethinylestradiol from oral contraceptive preparations, which may increase adverse effects from ethinylestradiol. If ethinylestradiol is used simultaneously in treatment with ascorbic acid, the patient should be monitored for adverse effects of ethinylestradiol.

Acetylsalicylic acid: In case of simultaneous use, there is an increase in the urinary excretion of ascorbic acid and a decrease in the excretion of acetylsalicylic acid. Acetylsalicylic acid has been found to reduce the absorption of ascorbic acid by approximately 1/3. These effects are dose-related and vitamin C supplementation may be necessary in people chronically using high doses of acetylsalicylic acid. When using low-dose acetylsalicylic acid for cardiovascular indications, it is not necessary to add vitamin C supplements.

Salicylic acid: Salicylates inhibit active transport through the intestinal wall.

Isoprenaline: The chronotropic effect of isoprenaline is reduced when administered simultaneously with ascorbic acid.

Alcohol: Alcohol consumption reduces blood levels of ascorbic acid. The effects of concurrent use are unknown.

Mexiletine: Renal excretion of mexiletine may be accelerated when high doses of ascorbic acid are administered simultaneously with mexiletine.

Barbiturates (Primidone): When given concomitantly with barbiturates (primidone), the urinary excretion of ascorbic acid may be increased.

Amphetamine and tricyclic antidepressants: Ascorbic acid reduced renal tubular reabsorption of amphetamines and tricyclic antidepressants.

Fluphenazine and other phenothiazines: Ascorbic acid has been reported to reduce the therapeutic effect of phenothiazines. Fluphenazine concentration may also decrease.

Corticosteroids: Corticosteroids increase vitamin C oxidation. However, it is not clinically significant.

Tetracyclines: Tetracyclines inhibit the intracellular metabolism of vitamin C and its reabsorption at the level of the renal tubules.

Amygdalin: One case has been reported of an increased risk of cyanide poisoning following simultaneous intake of high doses of vitamin C (>4000 mg) and amygdalin.

Aluminum: High doses of vitamin C taken with aluminum may cause increased reabsorption of aluminum. This interaction was not considered clinically significant in subjects with normal renal function.

In theory; High doses of vitamin C may cause acidification of the urine, resulting in unexpected renal tubular reabsorption of acidic drugs, thus exaggerating the response. On the other hand, basic drugs may show reduced reabsorption, resulting in decreased therapeutic effect.

Interactions with Food/Supplements

Iron: Vitamin C may increase iron absorption in people with iron deficiency. Small gradual increases in iron levels may be important in patients with hereditary hemochromatosis or in heterozygous carriers of this disease, as they may exacerbate iron overload.

Laboratory interactions

Since vitamin C is a strong reducing agent (electron donor), it may cause chemical interference in laboratory tests involving oxidation-reduction reactions, such as analyzes of glucose, creatinine, carbamazepine, uric acid and inorganic phosphate in urine and serum, and analysis of fecal occult blood. Using specific tests that do not rely on reducing properties or discontinuing extra dietary vitamin C will prevent undesirable interactions. Consult the manufacturer's information to determine whether vitamin C may interfere with the test.

Vitamin C can interfere with tests that measure urine and blood glucose, causing erroneous readings, but it has no effect on blood glucose levels. Consult the meter or test kit's instructions for use to determine whether vitamin C interacts and for guidance on accuracy in readings.

Vitamin C hinders the determination of serum transaminases and lactic dehydrogenase with the autoanalyzer device. It may affect some tests performed to determine occult blood and serum theophylline levels.

4.6. Pregnancy and lactation

General advise

Pregnancy category: C

Women of childbearing potential / contraception

Oral contraceptives reduce the endogenous serum level of vitamin C. Vitamin C at a dosage of 1 gram per day may increase the bioavailability of ethinylestradiol from oral contraceptive preparations, which may increase adverse effects from ethinylestradiol. If ethinylestradiol is used simultaneously in treatment with ascorbic acid, the patient should be monitored for adverse effects of ethinylestradiol.

Pregnancy period

Animal studies are insufficient regarding effects on pregnancy and/or birth and/or postnatal development (see. Section 5.3). The potential risk to humans is unknown. ASCORVİT should not be used during pregnancy unless deemed necessary by the physician.

Vitamin C is considered safe during pregnancy when taken at recommended doses. However, because there are no adequate controlled human studies evaluating the risk of vitamin C therapy during pregnancy, the product should be used during pregnancy only when recommended by a physician. The recommended dose should not be exceeded, as chronic overdose may be harmful to the fetus.

Lactation period

Ascorbic acid passes into breast milk. It is not known whether taking high doses has a harmful effect on the baby, but this is theoretically possible. Therefore, it is recommended that

breastfeeding mothers do not exceed the maximum daily requirement unless the expected benefit exceeds the potential risk.

Reproductive ability / Fertility
There is no evidence that vitamin C at normal endogenous levels causes adverse reproductive effects in humans. It is not known whether ASCORVİT affects reproductive ability.

4.7. Effects on ability to drive and use machines
ASCORVİT has no or negligible adverse effects on driving and using machines.

4.8. Undesirable effects
The evaluation of undesirable effects is based on the following frequencies:
Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

The following adverse reactions have been identified after approval of product use. Because these reactions are reported voluntarily, it is not possible to reliably estimate the frequency of events.

Blood and lymphatic system disorders:
Very Rare: Hemolysis in patients with G6PD (Glucose-6-phosphatase deficiency) when used above the recommended dose.

Immune system diseases
Very Rare: Allergic reaction, anaphylactic reaction, anaphylactic shock.

Rarely observed hypersensitivity reactions detected by relevant laboratory findings and clinical symptoms:

- allergic asthma syndrome
- includes mild to moderate reactions affecting the skin, respiratory tract, gastrointestinal tract and cardiovascular system, with symptoms such as rash, urticaria, allergic edema and angioedema, pruritus and cardio respiratory distress.

Nervous system diseases
Unknown: Headache, dizziness, fatigue, sleep disturbance

Gastrointestinal diseases
Very Rare: Diarrhea, nausea, vomiting, abdominal pain, dyspepsia

Skin and subcutaneous tissue diseases
Unknown: Flushing or redness

Musculoskeletal, connective tissue and bone disorders
Rare: Tenderness, pain, fever or swelling in the arms and legs

Kidney and urinary diseases
Rare: Difficulty urinating
Unknown: Diuresis, hyperoxaluria, and kidney stone formation in people with the potential to form kidney stones or when used above the recommended dose.

General disorders and administration site conditions
Unknown: Injection and infusion site reactions.

Reporting of suspected adverse reactions

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose and treatment

There is no evidence that this product can cause overdose when used as recommended.

Vitamin C intake from all other sources should be considered.

Clinical signs and symptoms, laboratory findings, and consequences of overdose are highly variable and depend on the individual's susceptibility and environmental conditions.

The general picture of vitamin C overdose is an increase in gastrointestinal disturbances, including diarrhea, nausea and vomiting.

If these symptoms occur, treatment should be discontinued and symptomatic treatment should be performed.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic Group: Ascorbic acid (Vitamin C) (Lean)
ATC Code: A11GA01

Vitamin C is a cofactor for various enzymes involved in collagen, carnitine, and neurotransmitter biosynthesis; It is a water-soluble antioxidant and increases the gastrointestinal absorption of dietary non-heme iron. Due to the body's low vitamin C storage capacity, people need to take adequate amounts of vitamin C regularly.

While marginal deficiency results in fatigue, feeling unhealthy, and impaired concentration, severe deficiency leads to weakening of collagen structures, resulting in tooth loss, joint pain and connective tissue diseases (impaired bone growth and unbalanced ossification), delayed wound healing and worsening immunity.

Vitamin C and its metabolite, dehydroascorbic acid, form a reversible redox system that participates in many enzymatic reactions and forms the basis of the vitamin C spectrum of action. Vitamin C is the major water-soluble antioxidant in human serum and plays a leading role in protecting plasma lipids and nucleic acids from free radicals generated during normal metabolism, as well as from damage due to exposure to toxins and environmental pollutants (e.g., smoking). Vitamin C is the only endogenous antioxidant that can completely protect all lipid classes against detectable peroxidative damage.

Vitamin C works as a cofactor by transferring electrons in a series of hydroxylation and amidation reactions to enzymes that provide reducing equivalents.

The importance of vitamin C to the human body is most clearly seen in clinically significant vitamin C deficiency, namely scurvy. Vitamin C plays an important role in producing hydroxyproline from proline, which is essential in the development of functionally active collagen. Symptoms seen in scurvy, such as delayed wound healing, bone growth disturbances, vascular fragility, and dentin formation diseases, are the result of impaired collagen formation.

Additionally, vitamin C concentrations in plasma and leukocytes decrease rapidly in cases of infection and stress. Vitamin C is important for leukocyte and macrophage functions, neutrophil motility, phagocytosis, antimicrobial activity, interferon synthesis, cell-mediated immune responses such as allergic reactions, and collagen synthesis and wound healing, which is important for the covering of all body openings and the physical barrier provided by the skin against infections. is necessary. Vitamin C contributes to maintaining the redox integrity of cells and thus protects them against reactive oxygen species generated during the respiratory burst and the inflammatory response. Vitamin C has antiviral properties. All these different properties of vitamin C contribute to its role in supporting immune functions. Increased vitamin C intake has been shown to benefit many groups at risk of infection and reduce the severity and duration of colds.

In summary, vitamin C (ascorbic acid) is an important water-soluble vitamin and antioxidant. Due to the body's low vitamin C storage capacity, people need to take adequate amounts of vitamin C regularly.

5.2. Pharmacokinetic properties

General Features

Absorption:

Ascorbic acid is absorbed predominantly in the upper small intestine via a sodium-dependent active transport mechanism. When ascorbic acid is present in high concentrations, absorption occurs through passive diffusion. After oral administration of doses up to 180 mg, up to 70-90% is absorbed. After administration of doses such as 1-12 g, the rate of absorbed ascorbic acid decreases from approximately 50% to 15%, but the absolute amount of absorbed substance continues to increase.

Distribution:

The binding rate of ascorbic acid to plasma proteins is approximately 24%. Serum concentrations are normally 10 mg/L (60 µmol/L). Concentrations below 6 mg/L (35 µmol/L) indicate that vitamin C intake is not always sufficient. Concentrations below 4 mg/L (20 µmol/L) indicate insufficient vitamin intake. In clinical ascorbic acid deficiency, serum concentrations are below 2 mg/L (10µmol/L).

Biotransformation:

Ascorbic acid is partially metabolized to oxalic acid via dehydroascorbic acid. However, when taken in excessive amounts, ascorbic acid is excreted largely unchanged in urine and feces. Ascorbic-acid-2-sulfate is also found in urine as a metabolite.

Elimination:

Physiological body stores are approximately 1500 mg. Excretion of ascorbic acid; Its half-life is related to the method of administration, the amount administered, and the rate of absorption.
After intravenous administration of 500 mg sodium ascorbate, the half-life is approximately 6 hours. When vitamin C is taken in amounts of 1-3 g, the main route of excretion is through the kidneys. In doses exceeding 3 g, increased amounts are excreted unchanged in the feces.

5.3 Preclinical safety data

No specific studies have been conducted on this product. Preclinical data reveal no special risk for humans based on studies of single and repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Methyl paraben (E218)
Propyl paraben (E216)
EDTA disodium
Sodium Hydroxide (pH adjuster)
Water for injection

6.2. Incompatibilities
Since there are no incompatibility studies, this product should not be mixed with other drugs.

6.3. Shelf Life
24 months

6.4. Special precautions for storage
Store at room temperature below 25°C, protected from light.

6.5. Nature and contents of container
The product, filled in colorless Type I glass ampoules, is packaged in a cardboard box with a plastic carrier blister containing 5 ampoules of 5 mL.

6.6. Special precautions for disposal and other handling
Unused products or waste materials should be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging Waste Control Regulations".

7. MARKETING AUTHORIZATION HOLDER
Haver Trakya İlaç San. ve Tic. A.Ş.
Ulaş OSB Mah. D100 Cad. No:28/1, Ergene 2 OSB
Ergene/TEKİRDAĞ
Phone: (0282) 655 55 05

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2018/268

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First authorization date: 15.05.2018
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10. DATE OF REVISION OF THE TEXT