

Ascorbic Acid Injection

Ascorbic Acid (Vitamin C) 500 mg/5 mL

Presentation

Ascorbic Acid Injection is a clear, colourless solution containing in each mL of injection; 100 mg ascorbic acid BP, 0.01 mL benzyl alcohol, 45 mg sodium bicarbonate BP, 8.5 mg sodium chloride BP/USP and 0.2 mg thiourea in water for injections. The pH of the solution is between 5.5 and 7.0.

Uses

Actions

Ascorbic acid (Vitamin C) is a water soluble vitamin.

Ascorbic acid is essential for the formation of intercellular collagen and therefore is required for the maintenance of tooth structures, bone matrix and the walls of capillaries. It is also believed to be important in oxidation-reduction reactions, tyrosine metabolism, conversion of folic acid to folinic acid, carbohydrate metabolism, synthesis of lipids and proteins, iron metabolism, resistance to infections, and cellular respiration.

The reducing properties of ascorbic acid make it a useful drug in the treatment of idiopathic methaemoglobinemia, as well as in its familiar role as an antioxidant in many pharmaceutical formulae and in foodstuffs.

Ascorbic acid facilitates the absorption of iron by keeping iron in the reduced form.

Its role in the management of the common cold and a variety of other disorders remains unsubstantiated.

Pharmacokinetics

Ascorbic acid is widely distributed in body tissues. Concentrations in leukocytes and platelets are higher than those in erythrocytes and plasma. About 25% of ascorbic acid in plasma is bound to protein.

Normal plasma concentrations of ascorbic acid are approximately 10 to 20 mcg/mL. Total body stores of ascorbic acid have been estimated to be about 1.5 g with about 30 to 45 mg turnover per day.

Ascorbic acid crosses the placenta and the cord blood concentration is generally 2 to 4 times the concentration in maternal blood.

Although ascorbic acid is primarily excreted unchanged, some metabolic pathways have been identified. One route of metabolism involves conversion of L-ascorbate to oxalate. Ascorbic acid-2-sulphate has also been identified as a metabolite in human urine.

Ascorbic acid in excess of bodily requirements is excreted, largely unchanged, in the urine. There is a renal threshold of about 14 mcg/mL, and increasing amounts of ingested ascorbic acid are excreted unchanged in the urine when the daily intake exceeds 200 mg.

The elimination half-life of ascorbic acid is variable and dose-dependent because of its non-linear pharmacokinetics. Ascorbic acid can be removed by haemodialysis.

Indications

Prevention and treatment of ascorbic acid deficiency (ie. scurvy) when oral therapy is contraindicated.

As a supplement during periods of increased requirements, only if needs cannot be met from normal dietary sources and oral supplemental therapy is contraindicated, eg. wound healing, burns, infections, trauma, post-operatively and in thyrotoxicosis.

As an adjunct in the treatment of idiopathic methaemoglobinaemia.

The use of ascorbic acid with desferrioxamine therapy to increase iron excretion remains unsubstantiated. Injectable ascorbic acid is administered for the above indications where oral administration is not possible, or in which medication given by the oral route will not be sufficiently absorbed.

Dosage and Administration

Parenteral ascorbic acid should only be used when oral therapy is contraindicated.

Ascorbic Acid Injection may be administered intramuscularly, subcutaneously, or intravenously. Intramuscular administration is preferred. The drug should be infused slowly when given by the intravenous route; rapid intravenous injection may cause temporary dizziness.

Therapeutic doses substantially exceed recommended dietary allowances. In adults, doses of 100 to 250 mg once or twice daily for several days are recommended to reverse the effects of scurvy. Doses up to 1 to 2 g may be given in extreme cases. In infants and children with scurvy, 100 to 300 mg/day in divided doses is recommended.

In idiopathic methaemoglobinaemia, 300-600 mg of ascorbic acid per day in divided doses has been recommended.

In pregnancy, the daily dose recommended is 60 mg, while in lactation 80 mg per day is recommended.

In adults, 45-60 mg of ascorbic acid daily is sufficient as a dietary supplement. Smokers may require 100 mg of ascorbic acid daily.

In adults undergoing chronic haemodialysis, 100-200 mg/day is recommended.

Contraindications

The injection is contraindicated in individuals who are hypersensitive to any of the ingredients within the preparation.

A fatal reaction believed to be related to the presence of benzyl alcohol as a preservative has been described in low birth weight neonates. The use of this product in this group is contraindicated.

Warnings and Precautions

Large doses of ascorbic acid elevate urinary oxalate levels and may precipitate the formation of calcium oxalate urinary calculi. Patients with impaired renal function and/or a history of renal stones can be more susceptible to this effect.

As ascorbic acid increases iron absorption, large doses can be dangerous in patients with haemochromatosis, thalassaemia, polycythemia, leukaemia or sideroblastic anaemia. Patients with iron overload should keep their ascorbic acid intake to a minimum.

Use with caution in patients with glucose-6-phosphate dehydrogenase deficiency as haemolysis has been known to occur with the use of ascorbic acid.

High doses of ascorbic acid has been associated with sickle-cell crisis in patients with sickle-cell anaemia.

Chronic use of high doses of ascorbic acid can lead to increased metabolism of the drug, in which case sudden reduction in dosage can give rise to symptoms of deficiency. If this occurs, higher dosage should be reinstated, and then withdrawn more slowly.

Pain and rarely thrombophlebitis, due to chemical irritation, can occur along the course of the vein when high potency vitamin solutions are infused too rapidly. Accordingly, the solution should be infused slowly and care should be taken to avoid extravasation during the infusion. As with all parenteral solutions, care must be taken not to overload the circulatory system, especially in cardiac or pulmonary disorders.

The diabetogenic effect of ascorbic acid remains controversial. However, blood glucose concentration should be monitored periodically in patients receiving prolonged treatment with Ascorbic Acid Injection, especially early in the course of therapy. Note: Ascorbic Acid Injection may interfere with some urinary glucose tests.

Theoretically, large doses of ascorbic acid may cause gouty arthritis in susceptible individuals due to its effect on uric acid excretion.

Ascorbic acid has been thought to aggravate rapidly proliferating and widely disseminating tumours. Therefore, caution should be exercised when prescribing ascorbic acid to patients with advanced cancer.

Use in pregnancy

The minimum daily requirement is increased to 60 mg in pregnant women during the second and third trimesters. Supplementary oral ascorbic acid should be taken if this amount cannot be met by dietary intake.

Ascorbic acid crosses the placenta. With the ingestion of high doses of ascorbic acid during pregnancy, the foetus can adapt and then develop a scorbutic illness after birth as a withdrawal reaction. Therefore, higher doses should not be used in pregnant women, or those likely to become pregnant, unless the expected benefits outweigh any potential risk.

Use in lactation

The minimum daily requirement is increased to 80 mg during lactation.

Ascorbic acid is excreted in the breast milk. A maternal diet containing adequate ascorbic acid is sufficient to prevent deficiency in breast fed infants, who therefore require no supplementation. (Most commercial formulas are enriched with ascorbic acid). It is not known whether maternal intake grossly in excess of the usual recommendation leads to harmful effects in the infant, but theoretically this could occur. Therefore it is recommended that nursing mothers do not exceed the maximum daily requirement unless the expected benefits outweigh any potential risk.

Adverse Effects

Hot flushes, headache, fatigue, insomnia, stomach cramp, nausea and vomiting.

Allergy to ascorbic acid is extremely rare. Four cases of respiratory and cutaneous allergies to ascorbic acid have been documented.

Transient pain and swelling at the site of subcutaneous or IM injection.

Too rapid intravenous injection can cause temporary dizziness or faintness.

Acidification of urine by large doses of ascorbic acid might cause precipitation of urate, oxalate or cystine stones or drugs in the urinary tract, especially since some ascorbate is metabolised to oxalate. Some patients with pre-existing renal disease have been reported to develop renal failure following treatment with high doses of ascorbic acid.

High dosage of ascorbic acid may cause diarrhoea.

Deep-vein thrombosis has been reported after large doses of ascorbic acid.

Rarely, decreased blood pH leading to sickle-cell crisis has been reported in patients with sickle cell disease.

At doses of greater than 600 mg, ascorbic acid has been reported to have a diuretic action.

High doses can increase serum cholesterol in atherosclerotic patients.

Interactions

Aspirin: Increased urinary excretion of ascorbic acid and decreased excretion of aspirin occur when the drugs are administered concurrently. Aspirin has been found to reduce the absorption of ascorbic acid by about a third.

Dicarmarol: An isolated case where the prothrombin time is reduced following intake of ascorbic acid.

Warfarin: Several cases have been reported in which ascorbic acid appeared to reduce the effect of warfarin.

Ethinylloestradiol: Ascorbic acid in a dosage of 1 g daily increases the bioavailability of ethinylloestradiol in oral contraceptive preparations. Thus, low dose contraceptives are made to resemble higher dose ones in their pharmacological and toxicological properties. This effect can be important if ascorbic supplementation is discontinued, as the drop in hormone absorption may lead to breakthrough bleeding or even contraceptive failure.

Iron (Oral): Ascorbic acid can increase absorption of iron.

Desferrioxamine: Ascorbic acid may increase the excretion of iron when given concomitantly with desferrioxamine. However, cases of cardiomyopathy and congestive heart failure have occurred in patients on concomitant treatment. It may be that ascorbic acid mobilises iron from spleen and other reticuloendothelial tissues resulting in increased iron deposition in visceral organs.

Isoprenaline: The chronotropic effect of isoprenaline decreases when administered concurrently with ascorbic acid.

Alcohol: Alcohol reduces ascorbic acid levels.

Disulfiram: Chronic use or high doses of ascorbic acid may interfere with the disulfiram - alcohol interaction when used concurrently.

Mexideline: High doses of ascorbic acid may accelerate renal excretion of mexideline when the drugs are administered concurrently.

Barbiturates or primidone: May increase urinary excretion of ascorbic acid when administered together with barbiturates or primidone.

Fluphenazine and other Phenothiazines: Ascorbic acid has been reported to decrease the therapeutic effect of phenothiazines. The concentration of fluphenazine may also be reduced.

Amphetamine and tricyclic anti-depressants: Ascorbic acid decreased renal tubular reabsorption of amphetamines and tricyclic anti-depressants.

Laboratory tests: Ascorbic acid interferes with laboratory tests involving oxidation and reduction reactions eg. glucose oxidase test, copper sulphate test due to its reducing properties. Ascorbic acid interferes with autoanalyser determination of serum transaminases and lactic dehydrogenase. It can also affect some tests for occult blood and serum theophylline levels.

Overdosage

Overdosage of ascorbic acid may cause acidosis and haemolytic anaemia in predisposed individuals eg. glucose-6-phosphate dehydrogenase deficiency. In massive ascorbic acid overdosage, renal failure may occur due to excessive oxalate excretion.

Treatment of Overdosage

In the event of overdosage, symptomatic or supportive measures should be taken.

On first sign of an allergic reaction, administration of ascorbic acid should be discontinued. For the treatment of allergic reactions, 0.5-1 mL of Adrenaline Injection BP (Adrenaline 1 in

1,000) can be administered intramuscularly, repeated every 10 minutes until improvement occurs. Antihistamines and corticosteroids by slow intravenous injection are a useful adjunctive measure.

Pharmaceutical Precautions

Store below 25°C. Protect from light. Ascorbic acid may undergo decomposition producing carbon dioxide. Therefore, ampoules containing Ascorbic Acid Injection should be opened carefully due to increased pressure which may develop especially after prolonged storage. Ascorbic Acid Injection should not be used if visible turbidity, discolouration or crystallisation occur.

Incompatibility

Ascorbic acid is reported to be incompatible with ferric salts, oxidising agents, and salts of heavy metals, particularly copper.

Injections of ascorbic acid are reported to be incompatible with aminophylline, bleomycin sulphate, erythromycin lactobionate, nafcillin sodium, doxapram hydrochloride, cephalosporin sodium, nitrofurantoin sodium, conjugated oestrogens, sodium bicarbonate, and sulphafurazole diethanolamine. Incompatibility, dependent on pH or concentration, has been reported with chloramphenicol sodium succinate, chlorothiazide sodium, hydrocortisone sodium succinate and penicillin G potassium.

Medicine Classification

General Sale Medicine

Package Quantities

500 mg 50 x 5 mL ampoules

Further Information

Not Applicable

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