New Zealand Datasheet

1 PRODUCT NAME

ASCOR L 500®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ascorbic acid 500 mg/ml

3 PHARMACEUTICAL FORM

Ascor L 500® (Ascorbic Acid Injection, USP) is a sterile, nonpyrogenic solution of ascorbic acid prepared with the aid of sodium bicarbonate in water for injection. Ascorbic Acid is an essential water-soluble vitamin. Ascor L 500® is a clear solution in an amber glass vial. Each ml contains 500 mg of ascorbic acid, and edetate disodium 0.025% (w/v).

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ascor L 500® is indicated for ascorbic acid deficiency. Parenteral ascorbic acid supplementation may be necessary in the treatment of scurvy for patients with gastric disorders, for patients with extensive injuries, for surgical patients and others only if their needs cannot be met from normal dietary sources or in patients who cannot take oral vitamins. Acute ascorbic acid deficiency may be associated with extensive injuries and other states of extreme stress. Vitamin C requirements are also significantly increased in certain diseases and conditions such as tuberculosis, hyperthyroidism, peptic ulcer, neoplastic disease, pregnancy and lactation.

4.2 Dose and method of administration

Ascor L 500® (Ascorbic Acid Injection, USP) is usually injected intramuscularly or subcutaneously.

The solution has a pH of 5.5 to 7.0 and is not usually irritating to the tissues. The solution also may be injected intravenously, but a higher percentage of the drug will be excreted in the urine than when the subcutaneous or intramuscular route is employed. When administered intravenously, Ascor L 500® should be slowly infused with large volume solutions. Ascor L 500® should be added to such solutions shortly before venoclysis; any of the mixture remaining after administration should be discarded.

It is difficult to establish an exact dosage of ascorbic acid suitable for the treatment of deficiencies. In general, therapeutic doses should substantially exceed the recommended daily dietary allowances for healthy persons: Adult males 19 years of age and beyond, 90 mg; adult females 19 years of age and beyond, 75 mg; boys 14 to 18 years of age, 75 mg; girls 14 to 18 years of age, 65 mg; boys and girls 9-13 years of age, 45 mg; children 4-8 years of age, 25 mg; children 1-3 years of age, 15mg; infants through 12 months of age, 6 mg/kg/day. The blood level of ascorbic acid in normal persons ranges from 0.4 to 1.5 mg/100 ml.

The usual therapeutic parenteral dose ranges from 100 to 250 mg (0.2 to 0.5 ml of Ascor L 500®), once or twice daily. If the deficiency is extreme, 1 to 2 g (2 to 4 ml) may be given. There is no appreciable danger from excessive dosage because superfluous amounts of the vitamin are rapidly excreted in the urine.

When extensive injuries are treated, ascorbic acid may be given if any doubt exists regarding previous nutrition with the vitamin. Doses of 1 to 2 g daily for 4 to 7 days may be given before operation in gastrectomy patients. Similar doses also have been used postoperatively to aid wound healing following extensive surgical procedures.

Directions for Dispensing: The pharmacy bulk package is for use in a pharmacy admixture service only. A single entry through the vial closure should be made with a sterile dispensing set or transfer device. Multiple entries will increase the potential for microbial and particulate contamination. Use aseptic technique, preferably in a laminar flow environment. Ascor L 500® contains no preservative. Any unused portion must be discarded within 6 hours.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, as the solution and container permit.

4.3 Contraindications

Ascor L 500® is contraindicated in those persons who have a known hypersensitivity to any component of this preparation.

4.4 Special warnings and precautions for use

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.

4.5 Interaction with other medicines and other forms of interaction

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.

Ethinyloestradiol: Ascorbic acid in a dosage of 1 g daily increases the bioavailability of ethinyloestradiol 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.

Aluminium antacids: Patients with kidney failure given aluminium antacids and oral citrate can develop a potentially fatal encephalopathy due to marked rise in blood aluminium levels. There is evidence that vitamin C may interact similarly.

Laboratory tests: Because ascorbic acid is a strong reducing agent, it interferes with numerous laboratory tests based on oxidation-reduction reactions. Diabetics taking more than 500 mg of ascorbic acid daily may obtain false readings of their urinary glucose test. No exogenous ascorbic acid should be ingested for 48 to 72 hours before amine-dependent stool occult blood tests are conducted because false negative results may occur.

4.6 Fertility, pregnancy and lactation

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.

4.7 Effects on ability to drive and use machines

No effect expected.

4.8 Undesirable 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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Symptoms
Large doses may cause gastrointestinal disorders including diarrhoea. Doses of 600mg or more daily have a diuretic action. 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
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.

For information on the management of overdose, contact the National Poisons Centre on 0800 POISON (0800 764 766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamins, ATC Classification: A11G A01

Ascorbic acid (vitamin C), a water-soluble vitamin, is an essential coenzyme for collagen formation, tissue repair and synthesis of lipids and proteins. It acts both as a reducing agent and as an antioxidant and is necessary for many physiologic functions, e.g., metabolism of iron and folic acid, resistance to infection, and preservation of blood vessel integrity. Signs and symptoms of early vitamin C deficiency include malaise, irritability, arthralgia, hyperkeratosis of hair follicles, nosebleed, and petechial hemorrhages. Prolonged deficiency leads to clinical scurvy.

5.2 Pharmacokinetic properties

Ascorbic acid is normally present in both plasma and cells. The absorbed vitamin is ubiquitous in all body tissues. The highest concentrations are found in glandular tissue, the lowest in muscle and stored fat. About 25% of ascorbic acid in plasma is bound to protein. Ascorbic acid is partially destroyed and partially excreted by the body. There is a renal threshold for vitamin C; the vitamin is excreted by the kidney in large amounts only when the plasma concentration exceeds this threshold, which is approximately 1.4 mg/100 ml. When the body is saturated with ascorbic acid, the plasma concentration will be about the same as that of the renal threshold; if further amounts are then administered, most of it escapes into the urine. When body tissues are not saturated and plasma concentration is low, administration of ascorbic acid results in little or no renal excretion.

A major route of metabolism of ascorbic acid involves its conversion to urinary oxalate, presumably through intermediate formation of its oxidized product, dehydroascorbic acid. The elimination half-life of ascorbic acid is variable and dose-dependent because of its non-linear pharmacokinetics. Large doses are rapidly excreted in the urine when in excess of the requirements of the body and after an intravenous dose, about 40% is excreted in 8 hours, which is increased to about 70% after tissue saturation. The amount of unchanged drug is dose dependent; in women the excretion of ascorbic acid appears to vary with the stage of the menstrual cycle and it is decreased when taking oral contraceptives. Ascorbic acid can be removed by haemodialysis.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each ml contains 500 mg of ascorbic acid, and edetate disodium 0.025% (w/v). It also contains sodium bicarbonate and may contain sodium hydroxide to aid in preparation and pH adjustment.

6.2 Incompatibilities

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, cephazolin 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.

6.3 Shelf life

Shelf life is 24 months (2 years) from manufacture. Protect from light.
Once opened, use immediately. Discard any unused contents.

6.4 Special precautions for storage

Store in refrigerator at 2º to 8ºC. Do not allow to stand at room temperature before use. Failure to follow this caution may lead to excessive pressure inside the vial. Protect from light. Do not administer unless solution is clear and container is intact.

CAUTION: Pressure may develop within the vial during storage. Exercise caution when withdrawing.

6.5 Nature and contents of container

Ascor L 500® (Ascorbic Acid Injection, USP), 500 mg/mL, is available in trays of twenty-five, 50 ml, sterile, pharmacy bulk bottles, containing no preservative.

6.6 Special precautions for disposal

Not applicable

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

21 January 2010

10 DATE OF REVISION OF THE TEXT

27 June 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information