



## Apo-Ascorbic Acid

### Ascorbic Acid 50mg, 100mg and 250mg tablets

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### Presentation

APO-ASCORBIC ACID 50mg tablets are white, round, 6.5mm in diameter, flat with beveled edges. Each tablet contains 50mg ascorbic acid and typically weighs 100mg.

APO-ASCORBIC ACID 100mg tablets are white, round, 7mm in diameter, flat with beveled edges with "APO" and scored on one side "ASC" over "100" on the other side. Each tablet contains 100mg of ascorbic acid and typically weighs 130mg.

APO-ASCORBIC ACID 250mg tablets are white round, 8.7mm in diameter, biconvex. Each tablet contains 250mg ascorbic acid and typically weighs 326mg

### 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, cartilage, bone matrix the walls of capillaries and wound healing. Ascorbic acid influences the formation of haemoglobin, erythrocyte maturation and certain immunological and biochemical reactions in the body. Vitamin C deficiency is rare in adults but may occur in infants, alcoholics or the elderly. Deficiency leads to the development of scurvy.

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 methaemoglobinaemia, as well as in its familiar role as an antioxidant in many pharmaceutical formulae and in foodstuffs. Although some studies suggest that antioxidants may be beneficial in disease prevention further study is required before antioxidant vitamins can be recommended for the prevention of cancer or cardiovascular disease

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 readily absorbed from the gastrointestinal tract and is widely distributed in the body tissues with higher concentrations in the liver, leukocytes, platelets, glandular tissue and the lens of the eye. 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 range from 10-20mcg/mL with levels of 1-1.5mcg/mL being associated with survy. Total body stores of ascorbic acid have been estimated to be about 1.5 g with about 30 to 45 mg turnover per day. Plasma concentrations of ascorbic acid rise as the dosage ingested is increased until a plateau is reached with doses of 90-150mg daily.

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.



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

### **Indications**

As a supplement during periods of increased requirements, only if needs cannot be met from normal dietary sources 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

### **Dosage and Administration**

In preventing vitamin deficiencies adequate dietary intake is preferred over supplementation whenever possible. A daily intake of about 45-60 mg has been recommended for adults. Smokers may require 100 mg of ascorbic acid daily.

#### **Prevention of Deficiency**

25-75mg daily

#### **Treatment of Deficiency**

100-250mg once or twice daily for several days is recommended to reverse the effects of scurvy for adults. Doses up to 1 to 2 g may be given in extreme cases.  
For children 100-300mg daily in divided doses

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

Requirements for vitamin C may be increased in pregnancy, lactation, the elderly, hyperthyroidism, fever, cold exposure, stress, infection, trauma, burns, smoking and exposure to certain medicines.

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

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

### **Contraindications**

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

### **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.



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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.

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.

APO-ASCORBIC ACID is presumed to be safe and unlikely to produce an effect on the ability to drive or use machinery

### **Use in Pregnancy and Lactation**

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.

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, heartburn stomach cramp, nausea and vomiting.



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

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 1g/day or greater 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. Salicylates inhibit uptake of vitamin C into leukocytes and platelets. The clinical significance of this effect is variable. Patients on high dose salicylate therapy should be evaluated for possible vitamin C deficiency if they exhibit the related signs and symptoms.

**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. However early on in treatment when there is excess tissue iron there is some evidence that ascorbic acid may worsen the iron toxicity particularly to the heart. Thus ascorbic acid should not be given for the first month after starting desferrioxamine 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.



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**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

Shelf life: 48 months from the date of manufacture

Store at or below 30°C. Protect from heat, light and moisture.

Keep container tightly closed

#### Incompatibility

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

### Medicine Classification

General Sale Medicine

### Package Quantities

APO-ASCORBIC ACID 100mg:

Bottles of 100 and 500 tablets.

APO-ASCORBIC ACID 50mg & 250mg are currently not marketed.



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### **Further Information**

References for datasheet

AFT Pharmaceuticals Ltd, Ascorbic Acid Injection datasheet. Date of preparation 02 April 2007  
Baxter Healthcare Ltd, Ascorbic Acid Injection datasheet from New Ethicals Compendium – 8<sup>th</sup>  
Edition. Date of preparation 07 June 2000.

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