	Biomedical Limited, 1, Ohimege Road, Industrial Estate, Ga-Imam, Ilorin, Kwara State		
	Doc No. BML/VCS/S002	Date rev 06/2020	Next rev date: 05/2025

Summary of Product Characteristics

For

Vitamin C syrup

(Ascorbic acid)

	Biomedical Limited, 1, Ohimege Road, Industrial Estate, Ga-Imam, Ilorin, Kwara State		
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1. NAME OF MEDICINAL PRODUCT

Biomedical Vitamin C syrup

2. QUALITATIVE AND QUANTITATIVE DESCRIPTION

Each 5ml of the syrup contains

Ascorbic acid 100mg

3. PHARMACEUTICAL FORM

A clear syrup yellow liquid with Orange and Lemon flavour in 100ml amber PET bottle with pilfer proof cap and graduated dose measurement cap to facilitate easy dosing

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Vitamin C is an effective preparation for the treatment, control, prevention and improvement of the conditions and symptoms from Vitamin C deficiency

4.2 Posology and method of administration

Posology

The safety and efficacy of Vitamin C syrup has been established in adults and paediatric populations when taken at the prescribed doses

Method of Administration

Age group	**Dose**
Up to 1yr	2.5ml 3 times daily
1-6yr	5ml 3 times daily
6-12yrs	10ml 3 times daily

Or as directed by the physician.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

- Oxalate urolithiasis, hyperoxaluria

- Iron storage disorders/iron overload (e. g. thalassemia, hemochromatosis, sideroblastic anemia, erythrocyte concentrate transfusions)

- Renal insufficiency

- Glucose-6-phosphate dehydrogenase deficiency/defect

- Children under 12 years of age: high doses of vitamin C

4.4 Special warnings and Precautions for Use

Renal insufficiency

Patients with impaired kidney function have a higher risk of oxalate precipitation in urine due to vitamin C supplementation. Therefore, a strict monitoring of renal function (e.g. GFR, albumin) should be done.

Patients with a predisposition for the formation of renal calculi are at risk for the development of calcium oxalate stones when using high-dose vitamin C. It is recommended not to exceed a daily vitamin C intake of 100-200 mg in patients with a history of recurrent kidney stone formation.

Each injection vial of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion contains 42.3 mmol (972 mg) sodium. This has to be taken into consideration by patients on a controlled sodium diet.

Adequate fluid intake has to be assured (approximately 1.5 – 2 l per day).

It is also recommended to avoid additional oxalate-rich foods during therapy with ascorbic acid.

In isolated cases, patients with a history of difficulty breathing (such as obstructive or restrictive bronchial and lung disease) may experience acute dyspnea when treated with high-dosed (≥ 7.5 g) of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion. Lower initial doses are therefore recommended in these patients.

4.5 Drug Interactions

Drugs which induce tissue desaturation of ascorbic acid include acetylsalicylic acid, nicotine from cigarettes, alcohol, several appetite suppressants, iron, phenytoin, some anti-convulsant drugs, the oestrogen component of oral contraceptives and tetracycline.

Large doses of ascorbic acid may cause the urine to become acidic causing unexpected renal tubular reabsorption of acidic drugs, thus producing an exaggerated response. Conversely, basic drugs may exhibit decreased reabsorption resulting in a decreased therapeutic effect. Large doses may reduce the response to oral anticoagulants.

It has been reported that concurrent administration of ascorbic acid and fluphenazine has resulted in decreased fluphenazine plasma concentrations.

Ascorbic acid given in addition to desferrioxamine in patients with iron overload to achieve better iron excretion may worsen iron toxicity, particularly to the heart, early on in the treatment when

there is excessive tissue iron. Therefore, it is recommended that in patients with normal cardiac function ascorbic acid should not be given for the

first month after starting desferrioxamine. Ascorbic acid should not be given in conjunction with desferrioxamine in patients with cardiac dysfunction.

Acetylsalicylic acid can, taken in combination with high dosed of ascorbic acid, reduce the absorption of ascorbic acid and decreases urinary excretion. The clinical importance of this is uncertain.

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.

Oral contraceptives lower serum levels of ascorbic acid.

Ascorbic acid is a strong reducing agent and interferes with numerous laboratory tests based on oxidation - reduction reactions. Specialised references should be consulted for specific information on laboratory test interferences caused by ascorbic acid.

Usually a timely distance of 1 day between administration of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion and the laboratory test should be considered.

Due to lack of comprehensive clinical data, higher dosages of vitamin C should take place time-displaced to chemotherapy or radiotherapy. Is vitamin C infused before the chemo-/radiotherapy, a temporal distance of 24 hours is recommended. If vitamin C is administered after chemo-/radiotherapy, an interval of at least 24 hours should be maintained. For chemotherapeutics with a half-life > 6 hours, an interval of 3-4 half- lives should be maintained

4.6 Pregnancy and Lactation

Pregnancy and breastfeeding:

Ascorbic acid crosses the placental barrier and is excreted in breastmilk.

Daily doses of 100 to 500 mg ascorbic acid should not be exceeded in pregnant women and nursing mothers. Due to its high vitamin C content, Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion is not suited for the use in pregnancy and lactation.

Fertility

There are no studies on the influence on fertility.

4.7 Effects on ability to drive and use machine

No studies on the effects on the ability to drive and use machines have been performed. However, if undesirable side effects occur (e.g dizziness, blurred vision), the ability to drive and use machines may be impaired.

4.8 Undesirable effects

Adverse events are categorized by frequency as follows:

Very common (≥ 1/10)

Common (≥ 1/100 to <1/10)

Uncommon (≥ 1/1,000 to <1/100)

Rare (≥ 1/10,000 to <1/1,000)

Very rare (<1/10,000),

Not known (cannot be estimated from the available data)

Respiratory, thoracic and mediastinal disorders:

Very rare: Respiratory hypersensitivity reactions, e.g. dyspnoea/respiratory distress.

Skin and subcutaneous tissue disorders:

Very rare: Cutaneous hypersensitivity reactions, e.g. exanthema, urticaria, pruritus.

Vascular disorders:

Very rare: Transient circulation problems (e.g. dizziness, nausea, cephalgia, impaired vision)

Infections and infestations:

Very rare: Reactions such as chills and elevated temperature were observed in patients with acute infections.

Gastrointestinal disorders:

Very rare: Large doses may cause gastrointestinal disorders, e. g. nausea, vomiting, diarrhoea.

Renal and urinary disorders:

Very rare: Large doses may result in hyperoxaluria and renal oxalate calculi may form if the urine becomes acidic.

Very rare: Doses of 600 mg or more daily have a diuretic action.

4.9 Overdose

For the risk of formation of renal calculi

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Ascorbic acid

ATC code: A11GA01

Ascorbic acid and dehydroascorbic acid form an important redox system.

Vitamin C acts, due to its reduction potential, as co-factor in numerous enzyme systems, e.g. in collagen formation, catecholamine synthesis, hydroxylation of steroids, tyrosine and exogenous substances, carnitine biosynthesis, tetrahydrofolic acid regeneration, peptide alpha-amidation – a.o. of peptide hormones and neuropeptides (e.g. ACTH and gastrin).

Ascorbic acid blocks the chain reactions induced by oxygen radicals in aqueous body compartments. The antioxidant activities are in close biochemical interactions with the activities of vitamin E, vitamin A and carotenoids.

5.2 Pharmacokinetics Properties

The pharmacokinetic profile of ascorbic acid depends on the dose and administration route.

Following **oral** administration, dose-dependent absorption of ascorbic acid in the small intestine by specific Na+-dependent transporters (SVCT1 and SVCT2) occurs in an energy-consuming reaction.

Intake amounts of 200 mg are the optimum because their steady-state bioavailability is 100%. With doses of more than one gram, the absorption is less than 50%. Parts of the unabsorbed amount are degraded to inorganic acids and CO_2 by the microbiome.

Renal excretion includes glomerular filtration followed by re-absorption in the proximal tubulus. The renal threshold is approximately 57 µ mol/l (equivalent to 1 mg/dl). Below this plasma concentration, the re-uptake of ascorbate from the primary urine is complete. When the plasma concentration exceeds the renal threshold, the amount of ascorbate lost in the urine rises.

Oral use of 1 gram ascorbic acid results in peak plasma concentrations of approximately 90 µ mol/l (equivalent to 1.6 mg/dl). Extremely high oral doses (3 g vitamin C 6 times per day) yield plasma levels of 220 µ mol/l (equivalent to 3.9 mg/dl) within a short time.

Parenteral use of ascorbic acid leads to considerably higher plasma levels (>2.3 mmol/l equivalent to 40 mg/dl following infusion of 7.5 g ascorbic acid/50 ml). Plasma half-life after high-dose infusion is, due to the renal clearance, between 1.5 and 2.5 hours in healthy subjects.

Cellular uptake of ascorbate is achieved in body tissues and colonic lumen by the same sodium-dependent ascorbate transporters SVCT1 or SVCT2 in an energy- dependent process. The ability of tissues for the uptake of ascorbate depends on the intracellular transporter concentration that varies in different tissue types. An additional transport mechanism is the uptake of oxidized ascorbate (dehydroascorbate) via glucose transporters (GLUTs). This process proceeds more rapid than the active ascorbate uptake and promotes the glutathione-dependent regeneration inside the cell.

5.3 Preclinical Safety Data

Ascorbic acid doses of up to 1 g/kg body weight do not have teratogenic or fetotoxic effects in rats and mice. The acute and subchronic LD_{50} following intravenous administration is more than 200

mg/kg bw in rats, guinea pigs and dogs. Ascorbic acid is excreted in breast milk and crosses the placental barrier by simple diffusion.

Use of higher ascorbic acid doses during pregnancy can result in a higher predisposition for the development of scurvy in the offspring

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sucrose, Methyl paraben, Sodium metabisulphite, Citric acid, Orange flavour, Lemon flavour, Riboflavin, Propylene glycol, Glycerol, Sodium bicarbonate

6.2 Incompatibilities

None

6.3 Shelf life

2 years

6.4 Special Precautions for Storage

Vitamin C syrup should be stored in a cool dry place at temperatures not more than 30^{o}C

6.5 Nature and Contents of Container

Plain Amber-coloured Polyethylene terephthalates (PET) bottle with ROPP cap placed inside a paperboard carton

6.6 Special Precautions for disposal

Container and/or any unused product should be disposed in accordance with the local requirement

7. MANUFACTURER

BIOMEDICAL LTD
1, Ohimege Road, Industrial Estate
Ilorin Kwara State, PMB 1449

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