SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 vial with 50 ml concentrate for solution for injection/infusion contains: 7.5 g ascorbic acid

Excipient with known effect:

Sodium bicarbonate (50 ml of the concentrate contains 972 mg sodium).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for injection/infusion.

Clear, light yellow solution.

The pH ranges from 6.2 to 7.0.

The osmolality is 1500-1700 mOsmol/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of clinical vitamin C deficiency states not amenable to dietary supply or oral replacement therapy.
Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion is indicated in adults.

4.2 Posology and method of administration

Posology

Adults:
The usual dose is 0.5 to 1.0 g ascorbic acid (corresponding to 3.3 – 6.7 ml concentrate). Severe trauma or surgery can require daily dosages of at least 3 g ascorbic acid to restore normal plasma levels. Depending on the disease situation, up to 7.5 g ascorbic acid (50 ml concentrate) per day may be used for infusion.

Paediatric population:
The safety and efficacy of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion in children and adolescents have not been established. No data are available.

Method of administration
For slow intravenous injection or infusion after dilution.
For instructions on dilution prior to administration, see section 6.6.
The injection/infusion therapy must be performed by a physician.

The duration of use depends on the course of the illness and the results of laboratory tests.

Instructions for handling:
The vial with preservative-free concentrate for solution for injection/infusion is for **single use** only. It has to be used immediately after opening. Any unused solution must be discarded.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Oxalate urolithiasis, hyperoxaluria
- Iron storage disorders/iron overload (e. g. thalassemia, hemochromatosis, sideroblastic anemia, erythrocyte concentrate transfusions)
- Renal insufficiency ***(KDIGO GFR stages G4 and 5 (< 30ml/min/1.73m^2)***
- Glucose-6-phosphate dehydrogenase deficiency/defect

4.4 Special warnings and precautions for use

Renal insufficiency (**KDIGO GFR stage G3 (30 to < 60 ml/min/1.73 m^2**)

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.

Note:

After the administration of gram doses, the ascorbic acid level in the urine may rise as much that the performance of tests for certain clinical-chemical parameters (glucose, uric acid, creatinine, inorganic phosphate) may be affected and the tests may yield false results. Testing for occult blood in the feces may also yield false-negative results.

Note to be considered in the treatment of diabetic patients:

Parenterally administered ascorbic acid interferes with the blood glucose determination assay.

4.5 Interaction with other medicinal products and other forms of interaction

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 Fertility, 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 machines

No studies on the effects on the ability to drive and use machines have been performed. However, if undesirable side effects occur as described in 4.8 (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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store .

4.9 Overdose

For the risk of formation of renal calculi see section 4.4.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ascorbic acid (vitamin C), plain

ATC code: A11GA01

Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion contains ascorbic acid, an active substance that is essential for the human body.

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 Pharmacokinetic 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 µmol/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 µmol/l (equivalent to 1.6 mg/dl). Extremely high oral doses (3 g vitamin C 6 times per day) yield plasma levels of 220 µmol/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

Sodium bicarbonate, water for injections.

6.2 Incompatibilities

A mixture with ascorbic acid solutions with reduction-sensitive substances should be avoided.

This medicinal product must not be mixed with other medicinal products, except those mentioned in section 6.6.

6.3 Shelf life

2 years.

The reconstituted/diluted product should be immediately used after reconstitution/dilution.

6.4 Special precautions for storage

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and contents of container

Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion is provided in a 50ml-amber glass (type II) injection vial with a stopper (butyl rubber), with a flip-cap (aluminium), containing 7.5 g of the active substance ascorbic acid.

6.6 Special precautions for disposal

Instructions for use/handling

The preservative-free concentrate for solution for injection/infusion is for **single** use only. It has to be used immediately after opening. Any unused solution must be discarded.

The osmolality of Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion is between 1500 and 1700 mOsmol/kg. Because osmolality for peripheral venous infusion should be below 800 mOsmol/kg, Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion must be diluted with isotonic NaCl solution in a ratio of 1:2, e.g. 50 ml Ascorbic Acid Pascoe 150 mg/ml Concentrate for solution for injection / infusion diluted with 100 ml isotonic NaCl solution.

7 MARKETING AUTHORISATION HOLDER

Pascoe pharmazeutische Präparate GmbH

Schiffenberger Weg 55

35394 Giessen

Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 14369/0009

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/02/2025

10 DATE OF REVISION OF THE TEXT

21/02/2025