Package Insert

a) Brand or Product Name

Pascorbin 7.5g,
150 mg/ml concentrate for solution for injection/infusion

b) Name and Strength of Active Substance(s)

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

Excipient with known effect:
Sodium hydrogen carbonate (50 ml of the product contains 972 mg sodium).

c) Product Description

Clear, light yellow solution.

d) Pharmacodynamics

Pharmacotherapeutic group: ascorbic acid (vitamin C), plain
ATC code: A11GA01

Pascorbin 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.

Sufficient vitamin E concentrations must always be ensured when high ascorbic acid doses are administered.

Risk populations:
At risk for vitamin C deficiency are elderly people (>65 years of age), regular heavy drinkers, smokers, pregnant women and nursing mothers and people with unbalanced dietary habits. Long-term use of medicines – salicylates, tetracyclines and corticosteroids in particular – may reduce the vitamin C reserves.

A massive drop of the vitamin C content in leukocytes and/or of vitamin C plasma concentrations is found in patients with acute infectious diseases, severe liver parenchyma disease, severe injuries (trauma, burns, major surgical procedures), acute pancreatitis, pneumonia, sepsis, multi-organ failure and during hemodialysis treatment. Low concentrations of vitamin C in plasma and leukocytes are also observed in patients with chronic infectious diseases, severe malabsorption syndromes and in end-stage malignant disease.

e) Pharmacokinetics

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 CO2 by the microbiome.

The renal clearance threshold is approximately 57 µmol/l (equivalent to 1 mg/dl). Energy-dependent re-uptake of ascorbate from the primary urine takes place only below this plasma concentration.

Oral use of 1 gram ascorbic acid results in peak plasma concentrations of approximately 90 µmol/l (equivalent to 1.4 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.

f) Indication

Treatment of clinical vitamin C deficiency states not amenable to dietary supply or oral replacement therapy.
Pascorbin is indicated in adults.

g) Recommended Dosage

Adults:
The usual dose is 0.5 to 1.0 g ascorbic acid (corresponding to 3.3 – 6.7 ml. 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) per day may be used for infusion.

The osmolarity of Pascorbin in is between 1500 and 1700 mOsmol/l. Because osmolarity for peripheral venous infusion should be below 800 mOsmol/l a dilution ratio of one part of Pascorbin plus 2 parts of a suitable isotonic carrier solution such as isotonic saline solution is recommended.

For volumes up to a maximum of 20 ml Pascorbin may be administered as an undiluted injection.
For volumes greater than 20 ml Pascorbin must be diluted with NaCL solution, Ringer´s solution or water for injection and administered as an infusion.
If NaCL solution or Ringer´s solution is used for the dilution of Pascorbin, the minimum dilution scheme is 1:2 (Pascorbin : carrier solution).
If water for injection is used for dilution, the minimum dilution scheme is 1:1 (Pascorbin : water for injection).
In both cases, i. e. dilution with NaCl-/ Ringer´s solution or water for injection, higher dilutions are also possible.

Paediatric population:
High doses of Pascorbin are contraindicated in children under 12 years. No data are available on the use of Pascorbin in adolescents.

h) Route of Administration
For intravenous use.
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.

i) Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section Name and Strength of Active Substance(s).
- 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/1.73m2)**
- Glucose-6-phosphate dehydrogenase deficiency /defect

j) Warnings and Precautions

Renal insufficiency (KDIGO GFR stage G3 (< 60 ml/min/1.73 m2)
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 Pascorbin 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 Pascorbin. 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 for diabetic patients:
Parenterally administered ascorbic acid interferes with the blood glucose determination assay.

k) Interactions with Other Medicaments

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 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.

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 Pascorbin and the laboratory test should be considered.

Due to lack of comprehensive clinical data, higher dosages of vitamin C therapy 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.

l) 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, Pascorbin is not suited for the use in pregnancy.

Fertility

There are no studies on the influence on fertility.

m) Side 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. dispnoea/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 side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03- 78835490, or visiting the website npra.moh.gov.my [Consumers→ Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

n) Symptoms and Treatment of Overdose

For the risk of formation of renal calculi see section Warnings and Precautions

o) 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 as described in section Side Effects (dizziness, blurred vision), the ability to drive and use machines may be impaired.

p) 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.

q) Incompatibilities and instruction for Use

A mixture with ascorbic acid solutions with reduction-sensitive substances should be avoided.
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

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.

r) Storage Conditions

Do not store above 30°C.
Keep the vial in the outer carton in order to protect from light.

Shelf life: 2 years.

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

s) Dosage forms and packaging available

Pascorbin 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.

t) Name and address of manufacturer/ product registration holder

Name and address of manufacturer
Pascoe pharmazeutische Präparate GmbH
Schiffenberger Weg 55
D-35394 Giessen
Germany

Product registration holder
Horizon Pharmaceuticals (Asia) Sdn. Bhd.
Jaya One Business Suites, Suite A-7-3A,
Jalan University, Section 13,
46200 Petaling Jaya,
Selangor, Malaysia

u) Date of revision of PI: 11.02.2026

v) Document name and revision number: Product Information_V03