APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

ASCORBIC ACID 500 mg/5 ml FRESENIUS solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 500 mg ascorbic acid.

Sugar free.

Excipients with known effect

Each 5 ml contains 66 mg of sodium.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

Colourless or pale-yellow solution.

The pH of the solution is between 5,5 and 7,0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ASCORBIC ACID FRESENIUS is administered by injection in severe deficiency states and where persistent vomiting, diarrhoea or other conditions prevent adequate utilisation by mouth.

4.2 Posology and method of administration

Posology

Doses of up to 1 g daily in divided doses have been recommended.

Prophylactic: 25 to 75 mg daily

Therapeutic: 200 to 600 mg daily

Children up to 5 years: 50 mg daily.

Method of administration

ASCORBIC ACID FRESENIUS may be administered, as sodium ascorbate, by the intramuscular route, and by the intravenous or subcutaneous routes.

4.3 Contraindications

- Hypersensitivity to ascorbic acid or to any of the excipients listed in section 6.1.
- Hyperoxaluria and the formation of renal calcium oxalate calculi.

4.4 Special warnings and precautions for use

ASCORBIC ACID FRESENIUS should be given with care to patients with underlying renal failure due to the risk of formation of renal oxalate calculi. Tolerance may be induced in patients taking high doses.

Large doses of ASCORBIC ACID FRESENIUS may result in haemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Very high doses of ASCORBIC ACID FRESENIUS may interfere with tests for sugar in the urine.

Monitoring of cardiac function has also been recommended for patients receiving combined

treatment with high doses of ASCORBIC ACID FRESENIUS and desferrioxamine.

ASCORBIC ACID FRESENIUS contains 66 mg sodium per 5 ml, equivalent to 3,3 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicines and other forms of interaction

Medicines which induce tissue desaturation of ascorbic acid include aspirin, nicotine from cigarettes, alcohol, several appetite suppressants, iron, phenytoin, some anticonvulsant medicines, the oestrogen component of oral contraceptives and tetracycline. Large doses of ASCORBIC ACID FRESENIUS may cause the urine to become acidic causing unexpected renal tubular reabsorption of acidic medicines, thus producing an exaggerated response. Conversely basic medicines may exhibit decreased reabsorption resulting in a decreased therapeutic effect. Large doses may reduce the response to oral anticoagulants.

There is evidence that the overall effect of a large supplement of ASCORBIC ACID FRESENIUS is to convert a low-oestrogen oral contraceptive into a high-dose oral contraceptive.

It has been reported that concurrent administration of ascorbic acid and fluphenazine has resulted in decreased fluphenazine plasma concentrations. Increased dosages of fluphenazine are necessary while under ASCORBIC ACID FRESENIUS treatment.

ASCORBIC ACID FRESENIUS 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.

ASCORBIC ACID FRESENIUS may increase the absorption of iron in iron-deficiency states.

ASCORBIC ACID FRESENIUS 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 FRESENIUS should not be given in conjunction with desferrioxamine in patients with cardiac dysfunction.

Aspirin can reduce the absorption of ASCORBIC ACID FRESENIUS by approximately a third and decreases urinary excretion by about half. 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Healthy foetal growth and development depends on a steady supply of nutrients from mother to foetus. However, high dosage of ASCORBIC ACID FRESENIUS throughout pregnancy may harm the foetus.

Breastfeeding

ASCORBIC ACID FRESENIUS crosses the placenta and is distributed into the breast milk.
High dosage of ASCORBIC ACID FRESENIUS while breastfeeding may be harmful to the baby and should be avoided.

4.7 Effects on ability to drive and use machines

ASCORBIC ACID FRESENIUS is unlikely to affect the patient's ability to drive a vehicle or use machinery

4.8 Undesirable effects

After the administration of ASCORBIC ACID FRESENIUS, the following side effects may occur:

Blood and lymphatic system disorders

Frequency unknown:

Reports of haemolysis in patients with glucose-6-phosphate dehydrogenase deficiency following large doses of ASCORBIC ACID FRESENIUS.

High doses of ASCORBIC ACID FRESENIUS may cause certain blood problems.

Gastrointestinal disorders

Frequency unknown:

Tolerance may be induced with prolonged use of large doses. Large doses are reported to cause diarrhoea and other gastrointestinal disturbances.

Renal and urinary disorders

Frequency unknown:

Renal impairment associated with excessive oxalate excretion has been reported following the administration of large doses of ASCORBIC ACID FRESENIUS.

General disorders and administration site conditions

Frequency unknown:

It has been stated that large doses may result in hyperoxaluria and the formation of renal calcium oxalate calculi.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of ASCORBIC ACID FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of ASCORBIC ACID FRESENIUS. Healthcare providers are asked to report any suspected adverse reactions via the **"6.04 Adverse Drug Reaction Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Healthcare providers are asked to report any suspected Adverse Drug Reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com, and to the relevant medicine's regulatory authority in the country where the product is marketed.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (See section 4.8). Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 22.1.4 (Vitamins)

ATC code: A11G A01

Ascorbic acid (Vitamin C), a water-soluble vitamin, is an essential factor in normal human nutrition. Ascorbic acid is essential for formation of collagen and intercellular material, and therefore necessary for the development of cartilage, bone, teeth and for the healing of wounds. It is also essential for the conversion from folic acid to folinic acid, facilitates iron

absorption from the gastrointestinal tract and influences haemoglobin formation and erythrocyte maturation.

Deficiency of ascorbic acid in the diet results in scurvy and other less serious conditions.

5.2 Pharmacokinetic properties

Distribution

Ascorbic acid is widely distributed in body tissues with about 25 % bound to plasma proteins. Large amounts are present in leucocytes and platelets. Ascorbic acid crosses the placenta.

Biotransformation

Ascorbic acid is oxidised to dehydroascorbic acid where some is metabolised to oxalic acid and the inactive ascorbate 2-sulphate. Metabolic turnover appears to be greater in females than males**.**

Elimination

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 medicine 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 is excreted in breast milk.

Oxalic acid and ascorbate 2-sulphate are excreted in the urine.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium bicarbonate (for pH-adjustment)

Water for injection.

6.2 Incompatibilities

Ascorbic acid is incompatible with alkalis, heavy metal ions, especially copper and iron, oxidizing materials, methenamine, phenylephrine hydrochloride, pyrilamine maleate, salicylamide, sodium nitrite, sodium salicylate, and theobromine salicylate.

In the absence of compatibility studies, this medicine must not be mixed with other medicines.'

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a dry place, at or below 25 °C.

Protect from light.

6.5 Nature and contents of container

Colourless or pale-yellow solution in 5 ml amber glass OPC ampoules.

Pack size of 10 x 5 ml ampoules are packed in trays as packed in cardboard containers.

6.6 Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8 APPLICATION NUMBER(S)

H2473 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION

Not applicable

10 DATE OF REVISION OF THE TEXT

23 January 2024