Professional Information for SUNFOZ

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SUNFOZ 3 g granules for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

- Each single dose sachet contains 3,0 g fosfomycin (as fosfomycin trometamol).
- Contains sugar: 2 153 mg sucrose per sachet.
- Contains sweetener: 16 mg saccharin sodium per sachet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules for oral solution.

Almost white mixture of powder and granules with citrus flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SUNFOZ is indicated as a single dose in the treatment of acute uncomplicated lower urinary tract infections caused by sensitive *E. coli*, in women and female children over the age of 12 years.

SUNFOZ is indicated for prophylaxis in diagnostic and surgical transurethral procedures in adult men.

4.2 Posology and method of administration

Posology

Adults:

The recommended dose for uncomplicated urinary tract infections in women, including the elderly up to seventy-five years, is a single 3 g dose.

The recommended dose for prophylaxis prior to transurethral surgical and diagnostic procedures in adult men, including the elderly, is two doses of 3 g. The first dose should be taken three hours before surgery. The second dose should be taken twenty-four hours after surgery.

Special populations

Paediatric population:

SUNFOZ in a dose of 3 g is not suitable for children under the age of 12 years.

Method of administration

SUNFOZ is administered orally as a single dose after reconstitution in water. SUNFOZ should be taken on an empty stomach at least 2 hours prior to the next meal, or about 2 – 3 hours after meals (see section 4.5).

The contents of a sachet should be dissolved in water and taken immediately after its preparation. For instructions on reconstitution of SUNFOZ before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to fosfomycin or to any of the excipients listed in section 6.1.
- Patients with severe renal insufficiency (CrCl < 10 mL/min).
- Patients undergoing haemodialysis.

4.4 Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship.

Hypersensitivity reactions:

Serious and occasionally fatal hypersensitivity reactions, including anaphylaxis and anaphylactic shock, may occur during fosfomycin treatment (see sections 4.3 and 4.8). If such reactions occur, treatment with SUNFOZ must be discontinued immediately and adequate emergency measures must be initiated.

Clostridioides difficile-associated diarrhoea:

Clostridioides difficile-associated colitis and pseudo-membranous colitis have been reported with fosfomycin and may range in severity from mild to life-threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of fosfomycin. Discontinuation of therapy with SUNFOZ and the administration of specific treatment for *Clostridioides difficile* should be considered. Medicines that inhibit peristalsis should not be given.

Persistent infections and male patients:

In case of persistent infections, a thorough examination and a re-evaluation of the diagnosis is recommended as this is often due to complicated urinary tract infections or the prevalence of resistant pathogens (e.g. *Staphylococcus saprophyticus*, see section 5.1). In general, urinary tract infections in male patients have to be considered as complicated UTIs for which SUNFOZ is not indicated (see section 4.1).

Paediatric population:

The safety and efficacy of SUNFOZ in children below 12 years of age have not been established. Therefore, SUNFOZ should not be used in this age group (see section 4.2).

Excipients:

Patients with rare hereditary problems of fructose intolerance, glucose- galactose mal-absorption or sucrase-isomaltase insufficiency should not take SUNFOZ.

4.5 Interaction with other medicines and other forms of interaction

Metoclopramide:

Concomitant administration of metoclopramide has been reported to lower serum and urinary concentrations of fosfomycin and should be avoided.

Other medicines that increase gastrointestinal motility may produce similar effects.

Food effect:

Food may delay the absorption of fosfomycin with consequent slight decrease in peak plasma levels and urinary concentrations. It is therefore preferable to take SUNFOZ on an empty stomach or about 2 – 3 hours after meals (also see section 4.2).

Specific problems concerning the alteration in International normalised ratio (INR):

Numerous cases of increased oral anticoagulant activity have been reported in patients receiving antibiotic therapy. Risk factors include severe infection or inflammation, age and poor general health. Under these circumstances, it is difficult to determinate whether the alteration in INR is due to the infectious disease or its treatment. However, certain classes of antibiotics are more often involved and in particular: fluoroquinolones, macrolides, cyclins, co-trimoxazole and certain cephalosporins.

Paediatric population:

Interaction studies have only been reported in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

No evidence in animals or humans has been reported to indicate adverse effects of fosfomycin in pregnancy. However, the safety and efficacy of single dose therapy has not been established for SUNFOZ in pregnancy.

Breastfeeding

SUNFOZ should not be given to lactating women. Fosfomycin has been reported to cross into breast milk.

Fertility

No effect on fertility has been reported in animal studies. No data have been reported in humans.

4.7 Effects on ability to drive and use machines

No specific studies have been reported, but patients should be informed that dizziness has been reported. This may influence some patients' ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

The most frequent reactions reported following the single-dose administration of fosfomycin involve the gastrointestinal tract, mainly diarrhoea. The events are usually self-limited in duration and resolve spontaneously.

Fosfomycin is generally well tolerated.

Tabulated list of adverse reactions

The following table displays adverse reactions that have been reported with the use of fosfomycin from either clinical-trial or post-marketing experiences.

System organ class	Frequency	Undesirable effect
Infections and infestations	Frequent	Vulvovaginitis
Immune system disorders	Frequency unknown	Anaphylactic reactions including anaphylactic shock, hypersensitivity (see section 4.4)
Nervous system disorders	Frequent	Headache, dizziness

Respiratory, thoracic and mediastinal disorders	Frequent	Pharyngitis (sore throat), rhinitis (runny or stuffy nose)
Gastrointestinal disorders	Frequent Less frequent Frequency unknown	Diarrhoea, nausea, dyspepsia (heartburn, indigestion), abdominal pain Vomiting Antibiotic-associated colitis (see section 4.4)
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Rash, urticaria, pruritus Angioedema
Musculoskeletal and connective tissue disorders	Frequent	Back pain
Reproductive system and breast disorders	Frequent	Vaginitis, Dysmenorrhoea
General disorders and administration site conditions	Frequent	Pain (non-localised), asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of SUNFOZ is important. It allows continued monitoring of the benefit/risk balance of SUNFOZ. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. *Suspected adverse reactions can also be reported directly to the Holder of certificate of registration email or telephonically: pharmacovigilance.africasme@sunpharma.com or tel: +27 (0) 12 643 2000*

4.9 Overdose

Experience regarding the overdose of oral fosfomycin is limited.

In the event of overdose, the patient must be monitored (particularly for plasma/serum electrolyte levels), and treatment should be symptomatic and supportive. Rehydration is recommended to promote urinary elimination of the active substance. Fosfomycin is effectively cleared from the body by haemodialysis with a mean elimination half-life of approximately 4 hours.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 20.1.1 Broad & medium spectrum antibiotics.

Pharmacotherapeutic group: Antibacterials for systemic use – other antibacterials.

ATC code: J01XX01.

Fosfomycin is a broad-spectrum bactericidal antibiotic, derived from phosphonic acid with activity in the lower urinary tract.

Mechanism of action

The antibacterial activity of fosfomycin is due to an inhibition of bacterial cell wall synthesis. Its particular mechanism of action is inhibition of enol pyruvyl transferase.

Mechanism of resistance

Main mechanism of resistance is a chromosomal mutation causing an alteration of the bacterial fosfomycin transport systems. Further resistance mechanisms, which are plasmid- or transposon-borne, cause enzymatic inactivation of fosfomycin by binding the molecule to glutathione or by cleavage of the carbon-phosphorus-bond in the fosfomycin molecule, respectively.

Cross-resistance:

Cross-resistance between fosfomycin and other antibiotic classes is not reported.

Susceptibility testing breakpoints:

The susceptibility breakpoints established by the European Committee on antimicrobial susceptibility testing are as follows (EUCAST breakpoint table version 11):

Species	**susceptible**	**Resistant**
Enterobacterales	≤ 8 mg/L	> 8 mg/L

Prevalence of acquired resistance:

The prevalence of acquired resistance of individual species may vary geographically and over time. Local information about the resistance situation is therefore necessary, particularly in order to ensure appropriate treatment of severe infections.

5.2 Pharmacokinetic properties

Absorption

Fosfomycin trometamol is an orally well-absorbed salt of fosfomycin. It usually provides therapeutic concentrations of the active moiety in the urine for periods of thirty-six hours or more from a single dose.

Biotransformation and elimination

Fosfomycin is eliminated mainly unchanged through the kidneys, and this results in very high peak urinary concentrations (approximately3 000 mg/L) within two to four hours. Therapeutic concentrations in urine are usually maintained for at least thirty-six hours. Food delays and reduces absorption of fosfomycin trometamol, resulting in reduced blood and urinary concentration.

Special populations

In patients with moderately reduced renal function (creatinine clearance >80 mL/min), including the physiological reduction in the elderly, the half- life of fosfomycin trometamol is prolonged but urinary concentration remains therapeutically adequate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Saccharin sodium (E954)

Natural orange flavouring 87D645 (containing maltodextrin, arabic gum [E414], citric acid [E330], sodium citrate [E331], butylated hydroxyanisole [E320])

Natural mandarin flavouring WONF 87D646 (containing maltodextrin, arabic gum [E414], citric acid [E330], sodium citrate).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened sachet:

24 months.

After reconstitution:

The reconstituted solution should be taken immediately.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the sachet in the outer carton until required for use.

6.5 Nature and contents of container

Three-layer polyethylene-aluminium-paper sachet supplied in an outer carton containing 1 sachet each.

6.6 Special precautions for disposal and other handling

The contents of one sachet must be dissolved in a glass of water. The solution should be taken immediately after being prepared. Any unused medicine should be disposed in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

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Roodepoort, 1724

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8. REGISTRATION NUMBER

57/20.1.1/0118

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20 August 2024

10. DATE OF REVISION OF THE TEXT

Namibia NS2 Reg.No.: 23/20.1.1/0060