PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1 NAME OF THE MEDICINE

FOMNOS 3 gram powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-dose sachet contains 5 631,0 mg fosfomycin trometamol, equivalent to 3,0 g of fosfomycin.

Excipients with known effect:

Contains sugar (2 193,0 mg sucrose) per sachet.

Contains sweetener (16,0 mg saccharin sodium) per sachet.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution.

Sachets containing white or off-white powder with orange flavour.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

FOMNOS 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.

FOMNOS 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.

Paediatric population

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

Method of administration

FOMNOS is administered orally as a single dose after reconstitution in water. To be taken at least two hours prior to the next meal.

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients with severe renal insufficiency (CLcr < 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 section 4.3 and 4.8). If such reactions occur,

treatment with fosfomycin 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 fosfomycin and the administration of specific treatment for *Clostridioides difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Paediatric population

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

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 this medicinal product is not indicated (see section 4.1).

Excipients

FOMNOS contains sucrose, which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take FOMNOS.

4.5. Interaction with other medicinal products and other forms of interaction

Metoclopramide

Concomitant administration of metoclopramide has been shown to lower serum and urinary concentrations of fosfomycin as in FOMNOS and should be avoided.

Other medicines that increase gastrointestinal motility may produce similar effects.

Food effect

Food may delay the absorption of the active ingredient of FOMNOS, with consequent slight decrease in peak plasma levels and urinary concentrations. It is therefore preferable to take the medicine on an empty stomach or about 2 to 3 hours after meals.

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 performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

FOMNOS should not be given to lactating women. Fosfomycin has been shown to cross into breast milk.

Fertility

No effect on fertility has been reported in animal studies. No data are available in human.

4.7. Effects on ability to drive and use machines

No specific studies have been performed 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

Adverse reactions are listed below by System Organ Class and frequency according to the MedDRA frequency convention and System Organ Classification.

The most common adverse reactions following the single-dose administration of fosfomycin involve the gastrointestinal tract, mainly diarrhoea. The following table displays ADRs that have been reported with the use of fosfomycin from either clinical trial or postmarketing experiences.

FOMNOS is generally well tolerated.

System Organ Class	**Adverse reaction**
	Frequency

	Frequent	**Less frequent**	**Frequency unknown**
Infections and infestations	Vulvovaginitis		
Immune system disorders			Anaphylactic reactions including anaphylactic shock, hypersensitivity (see section 4.4)
Nervous system disorders	Headache, dizziness		
Gastrointestinal disorders	Diarrhoea, nausea, dyspepsia (heartburn, indigestion), abdominal pain	Vomiting	Antibiotic-associated colitis (see section 4.4)
Skin and subcutaneous tissue disorders		Rash, urticaria, Pruritus	Angioedema

Reproductive system and breast disorders	Vaginitis, dysmenorrhoea		
Musculoskeletal and connective tissue disorders	Back pain		
Respiratory, thoracic and mediastinal disorders	Pharyngitis (sore throat), rhinitis (runny or stuffy nose)		
General disorders and administration site conditions	Pain (non- localised), asthenia		

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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

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

Pharmacotherapeutic group: antibacterials for systemic use - other antibacterials.

ATC code: J01XX01

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

Mode 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. Fosfomycin is active *in vitro* against species of gram-positive and gram-negative bacteria most frequently isolated in

urinary tract infections (*E. coli*, *Proteus*, *Klebsiella*, *Enterobacter*, *Staphylococcus* and *Streptococcus*). *In vitro* sensitivity does not necessarily imply *in vivo* efficacy.

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 (approx. 3 000 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

- Orange flavour: arabic gum (E414), BHA E320, dextrose monohydrate, ethyl butyrate, ethyl hexanoate, isoamyl acetate, isoamyl hexanoate, linalol, maltodextrine, natural citral 96 %, nerol, natural lemon essential oil 0,54 % and natural orange essential oil 3,06 %.
- Sucrose.
- Saccharin sodium.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

After reconstitution: The reconstituted solution should be used immediately.

6.4. Special precautions for storage

Store at or below 25 °C.

6.5. Nature and contents of container

Sachets are made of a high barrier laminate (Paper/Low Density Polyethylene/Aluminium/Low Density Polyethylene) and are supplied in an outer cardboard box containing 1 sachet.

6.6. Special precautions for disposal and other handling

The content of one sachet must be dissolved in 50 to 75 mℓ of water and the solution should be taken immediately after being prepared.

Any unused product or waste material should be disposed in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]
Waterfall 5-lr
Magwa Crescent West
Waterfall City
Jukskei View
2090

8. REGISTRATION NUMBER

52/20.1.1/0493

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 December 2020

10. DATE OF REVISION OF THE TEXT

Not applicable.

[1]Company Reg. No.: 1990/001979/07