Approved Professional Information for Medicines for Human Use:

FOSFOMYCIN 3 g CAMOX

Note: both the PI and PIL will be included in the packaging of this medicine.

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

FOSFOMYCIN 3 g CAMOX granules for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet contains fosfomycin trometamol equivalent to 3,0 g fosfomycin.

Excipient with known effect:

Contains sugar (sucrose: 2,213 g per sachet), see section 4.4.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules for oral solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

FOSFOMYCIN 3 g CAMOX 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 adolescents.

- for prophylaxis in diagnostic and surgical transurethral procedures in adult men.

4.2 Posology and method of administration

Posology

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.

Method of administration

FOSFOMYCIN 3 g CAMOX is administered orally after reconstitution in water. To be taken at least two hours prior to the next meal.

4.3 Contraindications

- Hypersensitivity to fosfomycin trometamol or to any of the excipients listed in section 6.1.
- severe renal insufficiency (creatinine clearance < 10 mL/min)
- patients undergoing haemodialysis.

4.4 Special warnings and precautions for use

Hypersensitivity

Hypersensitivity reactions, including anaphylaxis and anaphylactic shock, may occur during fosfomycin treatment and may be life-threatening (see section 4.8). If such reaction occurs, fosfomycin should never be re-administered and adequate medical treatment is required.

Antibiotic-associated diarrhoea

Antibiotic-associated diarrhoea (AAD) has been reported with use of nearly all antibacterial medicines, including fosfomycin, such as in FOSFOMYCIN 3 g CAMOX. AAD may range in severity from mild diarrhoea to fatal colitis. Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with FOSFOMYCIN 3 g CAMOX (including several weeks after treatment), may be symptomatic of *Clostridium difficile*-associated disease (CDAD). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with FOSFOMYCIN 3 g CAMOX. If CDAD is suspected or confirmed, appropriate treatment should be initiated without delay (see section 4.8). Anti-peristaltic medicines are contraindicated in this clinical situation.

Renal insufficiency

Urinary concentrations of fosfomycin remain effective for 48 hours after a usual dose if creatinine clearance is above 10 mL/min.

Paediatric population

Experience in children with fosfomycin 3 g is limited. FOSFOMYCIN 3 g CAMOX is not recommended for children below the age of 12.

Excipients: sucrose intolerance

FOSFOMYCIN 3 g CAMOX contains sucrose: patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take FOSFOMYCIN 3 g CAMOX.

4.5 Interaction with other medicines and other forms of interaction

Metoclopramide

Concomitant administration of metoclopramide has been shown to lower serum and urinary concentrations of fosfomycin and use of FOSFOMYCIN 3 g CAMOX with metoclopramide should be avoided.

Other medicines that increase gastrointestinal motility may produce similar effects.

Food

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

Alteration in INR

Numerous cases of increased antivitamin K antagonists activity have been reported in patients receiving antibiotics. 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, cotrimoxazole and certain cephalosporins.

4.6 Fertility, pregnancy and lactation

Pregnancy

No evidence in animals or humans has been found to indicate adverse effects of FOSFOMYCIN 3 g CAMOX in pregnancy. However, the safety and efficacy of single dose therapy has not been established for FOSFOMYCIN 3 g CAMOX in pregnancy.

Breastfeeding

FOSFOMYCIN 3 g CAMOX should not be given to breastfeeding 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 humans.

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.

4.8 Undesirable effects

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

System Organ Class (MedDRA)	***Frequent***	***Less frequent***	***Frequency not known***
Infections and infestations	Vulvovaginitis		
Immune system disorders			Anaphylactic reactions including anaphylactic shock, hypersensitivity
Nervous system disorders	Headache, dizziness		
Respiratory, thoracic and mediastinal disorders	Pharyngitis (sore throat), rhinitis (runny or stuffy nose).		
Gastrointestinal disorders	Diarrhoea, nausea, abdominal pain,	Vomiting	Antibiotic-associated

	dyspepsia (heartburn, indigestion)		colitis (see section 4.4)
Skin and subcutaneous tissue disorders	Skin rash	Urticaria, pruritus	Angioedema
Musculoskeletal and connective tissue disorders	Back pain		
Reproductive system and breast disorders	Dysmenorrhoea		
General disorders and administration site conditions	Pain (non-localised), asthenia		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

In the event of overdose, urinary elimination of fosfomycin can be accelerated through adequate administration of oral fluids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification/ Category and Class: A.20.1.1 Broad & Medium Spectrum Antibiotics

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.

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.

Inherently resistant species

Bacteroides spp.

Resistance

Main mechanism of resistance is a chromosomal mutation causing an alteration of the bacterial fosfomycin transport systems.

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.

Food delays and reduces absorption of fosfomycin trometamol, resulting in reduced blood and urinary concentrations.

Distribution

Fosfomycin is distributed to tissues including the kidneys and bladder wall. Fosfomycin is not bound to plasma proteins and crosses the placental barrier.

Biotransformation and elimination

Fosfomycin is eliminated mainly unchanged through the kidneys and this results in very high peak urinary concentrations (approx. 3000 mg/L) within two to four hours. Therapeutic concentrations in urine are usually maintained for at least thirty-six hours.

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 is prolonged but urinary concentration remains therapeutically adequate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mandarin flavour

Orange flavour

Sodium saccharin

Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original packaging until required for use.

Store at or below 25 °C.

6.5 Nature and contents of container

FOSFOMYCIN 3 g CAMOX granules are packed in sachets composed of surlyn/ aluminium/ low-density polyethylene/ paper. Each sachet contains white or almost white granules.

One or two sachets are packed in a cardboard box.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The dose must be dissolved in a glass of water and administered soon after dissolving.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBER

54/20.1.1/0077.076

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 May 2023

10. DATE OF REVISION OF THE TEXT