1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

TRACTINFECT 3 g powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of TRACTINFECT contains fosfomycin trometamol equivalent to 3 g fosfomycin.

Contains sugar: Sucrose 2,193 g

Contains sweetener: Saccharin sodium 16 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution

Single dose sachet containing white to off-white powder with orange flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TRACTINFECT is indicated:

- as a single dose in the treatment of acute uncomplicated lower urinary tract infections caused by sensitive *E. Coli*, in women 12 years and older.
- for prophylaxis in diagnostic and surgical transurethral procedures in adult men.
- for perioperative antibiotic prophylaxis for transrectal prostate biopsy 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 and for perioperative antibiotic prophylaxis for transrectal prostate biopsy in adult men, including the elderly, is two doses of 3 g. The first dose should be taken three hours before surgery or procedure. The second dose should be taken twenty-four hours after surgery or procedure.

Paediatric population

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

Method of administration

For oral administration.

TRACTINFECT should be taken on an empty stomach, either 1 hour before or at least 2 hours after meals and preferably before bedtime after emptying the bladder.

For instructions on reconstitution of the medicine before administration, see section 6.6.

Appearance of the product dissolved in water: clear to slightly opalescent, white solution, orange flavoured, free from undissolved particles.

4.3 Contraindications

TRACTINFECT is contraindicated in:

- Patients with hypersensitivity to fosfomycin trometamol or to any excipients in TRACTINFECT (see section 6.1).

- Severe renal insufficiency (creatinine clearance < 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 treatment with TRACTINFECT (see sections 4.3 and 4.8). If such reactions occur, treatment with TRACTINFECT must be discontinued immediately and adequate emergency measures must be initiated.

Elderly and patients with renal impairment

Fosfomycin trometamol, as contained in TRACTINFECT, is principally excreted by the kidney. Caution should be exercised in administering this antibiotic to patients with impaired renal function (see sections 4.3 and 5.2).

Pseudomembranous colitis

Antibiotic associated colitis (including pseudomembranous colitis) has been reported in association with the use of broad-spectrum antibiotics including TRACTINFECT. It is important to consider this diagnosis in patients who develop serious diarrhoea during or after the use of TRACTINFECT. In this situation adequate therapeutic measures should be initiated immediately. Medicines inhibiting peristalsis are contraindicated in this situation.

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).

Paediatric population

Safety and efficacy in children under the age of 12 years has not yet been established.

Sucrose intolerance

TRACTINFECT contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take TRACTINFECT.

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 and should be avoided.

Other medicinal products that increase gastrointestinal motility may produce similar effects.

Food effect

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

Specific problems concerning the alteration in INR

Studies indicate 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, cotrimoxazole and certain cephalosporins.

4.6 Fertility, pregnancy and lactation

The safety and efficacy of single dose therapy has not been established for TRACTINFECT in pregnancy. TRACTINFECT should not be given to lactating women.

Pregnancy

No evidence in animals or humans has been found to indicate adverse effects of TRACTINFECT in pregnancy.

Breastfeeding

Fosfomycin, as contained in TRACTINFECT, has been shown to cross into breast milk.

Fertility

No clinical data are available; hence the potential risk for humans is unknown.

4.7 Effects on ability to drive and use machines

TRACTINFECT has moderate influence on the ability to drive and operate machinery.

No studies on the effect on the ability to drive and use machines have been performed.

However, there are some side effects such as dizziness and fatigue associated with this product that may affect some patients' ability to drive or use machinery (see section 4.8).

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that TRACTINFECT do not adversely affect their ability to do so safely (see section 4.8).

4.8 Undesirable effects

a) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown (cannot be established from the available data)
Immune system disorders			Anaphylactic shock, allergic reaction
Nervous system disorders	Headache, dizziness	Paraesthesia	
Cardiac disorders		Tachycardia	
Vascular disorders			Hypotension
Respiratory, thoracic and mediastinal disorders	Pharyngitis, rhinitis		Asthma
Gastrointestinal disorders	Diarrhoea, nausea, abdominal pain, dyspepsia	Vomiting	Pseudomembranous colitis
Skin and subcutaneous tissue disorders	Skin rash	Urticaria, pruritus, itching	Angioedema
Musculoskeletal and connective tissue disorders	Back pain		
Reproductive system and breast disorders	Vaginitis, dysmenorrhea, vulvovaginitis		
General disorders and administrative site conditions	Pain (non-localised), asthenia	Fatigue	

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 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

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

The following events have been observed those who have taken fosfomycin in overdose: vestibular loss, impaired hearing, metallic taste and general decline in taste perception.

Treatment

In the event of overdose, treatment should be symptomatic and supportive. Urinary elimination of the medicine can be accelerated through adequate administration of oral fluids.

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

Mechanism of action

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 mechanism of action is inhibition of enol pyruvyl transferase, which catalyses the formation of n-acetylmuramic acid from n-acetyl aminoglucose and phosphoenolpyruvate. N-acetylmuramic acid is required for the build-up of peptidoglycan, an essential component of the bacterial cell wall. Fosfomycin has a mainly bactericidal action.

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, 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 activity moiety in the urine for periods of thirty-six hours or more from a single dose.

Distribution

These doses give peak plasma concentrations after 2 hours of 20 to 30 mcg/mL, serum half-life is largely independent of dose.

Elimination

Fosfomycin is eliminated mainly unchanged through the kidneys and this results in very high peak urinary concentrations (approximately 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 concentrations.

Renal impairment

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

Orange flavour, saccharin sodium, sucrose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

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

The powder is packed in sachets made of paper, low density polyethylene and aluminium foil.

Each sachet is packed in an outer cardboard carton.

6.6 Special precautions for disposal and other handling

No special requirements.

The contents of a sachet should be dissolved in a glass of water and taken immediately after its preparation.

Appearance of the product dissolved in water: clear to slightly opalescent, white solution, orange flavoured, free from undissolved particles.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8 REGISTRATION NUMBER

48/20.1.1/0482

9 DATE OF FIRST AUTHORISATION

02 February 2021

10 DATE OF REVISION OF TEXT

17 October 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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