PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

UTICIDE, 3 g granules for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains fosfomycin trometamol equivalent to 3 g fosfomycin.

Excipient with known effect:

Contains sugar (sucrose). One sachet contains 2,213 g sucrose. See section 4.4.

Contains sweetener (saccharin). One sachet contains 0,016 g.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules for oral solution.

White or almost white granules without lumps or particulates.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

UTICIDE is indicated as a single-dose in the treatment of acute uncomplicated lower urinary tract infections caused by sensitive *E. coli* in women and adolescent women.

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

4.2 Posology and method of administration

Posology

Women and adolescent women (> 12 years of age):

The recommended dose for uncomplicated urinary tract infections in women, including the elderly up to 75 years, is a single 3 g dose.

Adult men:

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 3 hours before surgery. The second dose should be taken 24 hours after surgery.

Children:

UTICIDE 3 g is not suitable for children between the ages of 5 and 12 years, as the recommended dose for this age group is a single 2 g dose and the sachet contents cannot be divided.

Method of administration

UTICIDE is taken orally, immediately after reconstitution in a glass of water. It should be taken at least 2 hours before the next meal, on an empty stomach.

4.3 Contraindications

Hypersensitivity to fosfomycin or to any of the excipients of UTICIDE (see section 6.1);

Patients with severe renal insufficiency (creatinine clearance < 10 ml/min);

Patients undergoing haemodialysis.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

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

Antibiotic-associated diarrhoea and *Clostridium difficile*-associated disease (CDAD)

Antibiotic-associated diarrhoea has been reported and may range in severity from mild diarrhoea to fatal colitis. Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with UTICIDE (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 severe diarrhoea during or after treatment with UTICIDE.

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.

Use in children

UTICIDE 3 g is not recommended for children under the age of 12 years (see section 4.2).

Information on the excipients

UTICIDE contains sucrose and saccharin (see section 2).

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

4.5 Interactions 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 should be avoided.

Other medicines that increase gastrointestinal motility may produce similar effects.

Alteration in international normalised ratio (INR)

Many cases of increased antivitamin-K antagonist activity have been reported in patients receiving antibiotics, including UTICIDE. Risk factors include severe infection or inflammation, age and poor general health.

Food

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

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

Fosfomycin is excreted into human milk. UTICIDE should not be given to lactating women.

4.7 Effects on ability to drive and use machines

Patients should be informed that dizziness has been reported. This may influence some patients' ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

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.

List of adverse events

Infections and infestations

Frequent: Vulvovaginitis

Frequency unknown: Antibiotic-associated colitis, pseudomembranous colitis

Blood and the lymphatic system disorders

Frequency unknown: Agranulocytosis, aplastic anaemia, eosinophilia, granulocytopenia, leucopenia, pancytopenia, and thrombocytopenia

Immune system disorders

Frequency unknown: Angioedema, anaphylactic reactions including anaphylactic shock, hypersensitivity

Nervous system disorders

Frequent: Headache, dizziness

Frequency unknown: Optic neuritis

Respiratory, thoracic and mediastinal disorders

Frequent: Pharyngitis, rhinitis

Frequency unknown: Exacerbation of asthma

Gastrointestinal disorders

Frequent: Diarrhoea, nausea, dyspepsia, abdominal pain

Less frequent:	Vomiting
Frequency unknown:	Antibiotic-associated colitis (see section 4.4), toxic megacolon

Hepatobiliary disorders

Frequency unknown:	Cholestatic jaundice, hepatic necrosis

Skin and subcutaneous tissue disorders

Less frequent:	Rash, urticaria, pruritus

Musculoskeletal, connective tissue and bone disorders

Frequent:	Back pain

Reproductive system and breast disorders

Frequent:	Dysmenorrhoea, vaginitis

General disorders and administration site conditions

Frequent:	Pain (non-localised), asthenia

Investigations

Frequency unknown:	Increases in serum concentration of aminotransferases, alkaline phosphatase and bilirubin

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. Health care 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/health-products-vigilance/. Reporting can also be done directly to Unicorn Pharmaceuticals at: vigilance@unicornpharma.co.za.

4.9 Overdose

No information is available on the overdose of oral fosfomycin.

In the event of overdose, side effects can be precipitated and/or be of increased severity (refer section 4.8).

In the event of overdose, treatment should be symptomatic and supportive. Rehydration is recommended to promote urinary elimination of the medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.1 Broad and 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 mechanism of action is inhibition of enol pyruvyl transferase.

Resistance:

The 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 36 hours or more from a single dose.

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

Biotransformation and elimination

Fosfomycin is eliminated mainly unchanged through the kidneys and this results in very high peak urinary concentrations (approximately 3 000 mg/L) within 2 to 4 hours. Therapeutic concentrations in urine are usually maintained for at least 36 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

Sucrose

Saccharin sodium

Mandarin flavour

Orange flavour.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store all medicines out of reach of children.

Store at room temperature (at or below 25 °C).

6.5 Nature and contents of the container

UTICIDE is packed in a four layered (surlyn/aluminium/low-density polyethylene/paper) sachet.

Sachets are supplied in cartons containing 1 or 2 sachets.

Not all packing sizes may be marketed at any one time.

6.6 Special precautions for disposal and other handling

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

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBER

53/20.1.1/0574

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

TBCDATE OF REVISION OF THE TEXT

Not applicable