Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Trimethoprim 10 mg/ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of oral suspension contains 10mg trimethoprim

Excipients with known effect
Liquid maltitol, 400mg per ml
Methyl hydroxybenzoate sodium, 1.72 mg per ml
Propyl hydroxybenzoate sodium,0.45 mg per ml
Sodium, 1.44mg per ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension.
White opaque suspension with odour of aniseed.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections and prophylaxis of recurrent urinary tract infections. Trimethoprim is indicated in adults and children aged over 12 years and children under 12 years (>6 weeks to <12 years old).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

1. Treatmentofrespiratoryandurinarytractinfections

Adults and children over 12 years: The usual dose is 200 mg (four 5ml syringes) twice daily for 7-10 days.

Children under 12 years: Based on 6mg/kg/day in two divided dosages as follows:
6 weeks to 5 months: 25 mg (half a 5ml syringe) twice daily for 7-10 days.

6 months to 3 years (8-15kg): 25-50 mg (half to one 5 ml syringe) twice daily for 7-10 days.

4-7 years (15-25kg): 50-75mg (one to one-and-a-half 5ml syringes) twice daily for 7-10 days.

8-12 years (25-40kg): 75-125mg (one-and-a-half to two-and-a-half 5ml syringes) twice daily for 7-10 days.

The first dosage on the first day can be doubled.

2. Prophylaxisofrecurrenturinarytractinfection:

Adults and children over 12 years: The usual dose is 100 mg (two 5ml syringes) at night.
An extra 100mg may be taken in the morning, if necessary.

Children under 12 years: 2.5mg/kg/day once daily in the evening.

3. Dosageinrenalimpairment

eGFR(ml/min)	Dosageadvised
Over 30	Normal
15-30	Normal for 3 days then half dose
Under 15	Half the normal dose

Monitoring of renal function and serum electrolytes should be considered particularly with longer term use, in patients with impaired renal function.

Trimethoprim should only be initiated and used in dialysis patients under close supervision from specialists in both infectious disease and renal medicine. Trimethoprim is removed by dialysis.

Monitoring trimethoprim plasma concentration may be considered with long term therapy but the value of this in individual cases should first be discussed with specialists in infectious disease and renal medicine.

Paediatric population
Trimethoprim is contraindicated in premature infants and neonates under 6 weeks, see section 4.3.

Methodofadministration
For oral use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Pregnancy (see section 4.6)

- Premature infants and neonates under 6 weeks
- Blood dyscrasias

4.4 Special warnings and precautions for use

Trimethoprim may cause a depression of haemopoiesis. During long-term therapy haematology should be monitored regularly in order to detect possible pancytopenia.

Particular attention should be paid to patients showing a tendency to folate deficiency, which may be aggravated by the use of this agent. If there is evidence of folic acid deficiency, calcium folinate should be administered and adequate response should be ensured by appropriate haematological monitoring. This treatment may not be effective unless trimethoprim is discontinued.

In patients with impairment of renal function, care should be taken to avoid accumulation. Monitoring of renal function and serum electrolytes should be considered particularly with longer term use. Trimethoprim should only be initiated and used in dialysis patients under close supervision from specialists in both infectious disease and renal medicine.

Special monitoring of serum electrolytes should be performed in risk patients due to risk of hyperkalaemia. See section 4.8.

Blood glucose should be monitored if used concomitantly with repaglinide (see Section 4.5).

Elevations in serum potassium have been observed in some patients treated with trimethoprim. Special monitoring of serum electrolytes should be performed in risk patients due to risk of hyperkalaemia, see section 4.8. Patients at risk for the development of hyperkalaemia include those with renal insufficiency, poorly controlled diabetes mellitus, or those using concomitant potassium- sparing diuretics, potassium supplements, potassium- containing salt substitutes, renin angiotensin system inhibitors (e.g.: ACE inhibitors or renin angiotensin receptor blockers), or those patients taking other drugs associated with increases in serum potassium (e.g. heparin). If concomitant use of the above- mentioned agents is deemed appropriate, monitoring of serum potassium is recommended (see section 4.5).

Prolonged use of an anti-infective may result in the development of super infection due to organisms resistant to that anti-infective.

Excipients

This medicine contains liquid maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

This medicine contains 1.72 mg of methyl hydroxybenzoate sodium and 0.45 mg of propyl hydroxybenzoate sodium per ml. May cause allergic reactions (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Folate antagonists and anticonvulsants: Trimethoprim may induce folate deficiency in patients predisposed to folate deficiency such as those taking folate antagonists or anticonvulsants. See section 4.4.

Bone marrow depressants: Trimethoprim may increase the potential for bone marrow aplasia. Cytotoxics such as azathioprine, mercaptopurine, methotrexate increase the risk of haematological toxicity when given with trimethoprim. See section 4.4.

Phenytoin and digoxin: Careful monitoring of patients treated with digoxin or phenytoin is advised as trimethoprim may increase plasma concentration of digoxin and phenytoin by increasing their elimination half-life.

Diuretics: In elderly patients concurrently taking diuretics, primarily thiazides, an increased incidence of thrombocytopenia with purpura has been reported. Rare cases of hyponatraemia have been reported in patients treated with trimethoprim and potassium sparing diuretics and/or thiazide diuretics.

Concomitant use of drugs that may increase serum potassium levels may lead to a significant increase in serum potassium. Potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, renin-angiotensin system inhibitors (e.g.: ACE inhibitors or renin angiotensin receptor blockers) and other potassium increasing substances (e.g.: heparin). Monitoring of potassium should be undertaken as appropriate (see section 4.4).

Ciclosporin: Ciclosporin may increase nephrotoxicity of trimethoprim.

Anticoagulants: The anticoagulatory effect of warfarin and other coumarins may be increased when taken together with trimethoprim.

Procainamide: Trimethoprim increases plasma concentration of procainamide.

Lamivudine: Trimethoprim may increase the plasma concentration of lamivudine.

Oestrogens: Trimethoprim may possibly reduce the contraceptive effect of oestrogens.

Oral typhoid vaccine: This is inactivated by concomitant administration of anti- bacterials.

Pyrimethamine: The anti-folate effect may be increased if there is concomitant administration with trimethoprim.

Dapsone: Plasma concentrations of trimethoprim and dapsone may increase when taken together.

Repaglinide: Trimethoprim may enhance the effect of repaglinide (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy
Trimethoprim is contraindicated during pregnancy, see section 4.3.

Breast-feeding

Trimethoprim is excreted in breast milk. Trimethoprim is contraindicated in premature infants and neonates under 6 weeks, see section 4.3. This should be kept in mind when considering administration to breast feeding women.

4.7 Effects on ability to drive and use machines

Trimethoprim has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequencies of the undesirable effects listed below are not known (cannot be estimated from the available data).

Infections and infestations
Aseptic meningitis.

Blood and lymphatic system disorders
Depression of haemopoiesis (see sections 4.4 and 4.5).

Immune system disorders
Hypersensitivity, anaphylaxis.

Metabolism and nutrition disorders
Hyperkalaemia, especially in patients with impaired renal function and in elderly patients. (see sections 4.4)

Eye disorders
Uveitis.

Gastrointestinal disorders
Nausea, vomiting, gastrointestinal upset.

Hepatobiliary disorders
Disturbances of liver enzyme values, jaundice.

Skin and subcutaneous tissue disorders:
Pruritus, skin rash, photosensitivity, angioedema.
Erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis

Musculoskeletal and connective tissue disorders
Myalgia.

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 professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie

4.9 Overdose

Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Trimethoprim and derivatives, ATC code: J01EA01. Trimethoprim is an antimicrobial agent.

Mechanism of action
The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

*In-vitro*trimethoprim has effect on most Gram-positive and Gram- negative aerobic organisms, including enterobacteria - *E.coli,Proteus,Klebsiellapneumoniae, Streptococcusfaecalis,Streptococcuspneumonia,Haemophilusinfluenzae,*and *Staphylococcusaureus.*

It has no effect on *Mycobacteriumtuberculosis,Neisseriagonorrhoeae,Pseudomonas aeruginosa,Treponemapallidum,*or anaerobic bacteria.

5.2 Pharmacokinetic properties

Absorption and Biotransformation
Trimethoprim is absorbed rapidly and almost completely following oral administration and maximal plasma concentrations are reached after 1-4 hours. Peak plasma concentrations of about 1 microgram per ml have been reported after a single dose of 100mg.

The half-life is about 12 hours in patients with normal renal function but up to 20-50 hours in anuric patients.

Distribution
Trimethoprim is rapidly and widely distributed to various tissues and fluids, including kidneys, liver, spleen, bronchial secretions, saliva and prostatic tissue and fluid, and the tissue concentrations are generally higher than the plasma concentration.

Excretion
Trimethoprim is predominantly excreted in the urine in unchanged form. Urinary concentrations are generally well above the MIC of common pathogens for more than 24 hours after the last dose.

5.3 Preclinical safety data

Not relevant (widely used in clinical practice).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose and Carmellose sodium
Xanthan gum
Methyl hydroxybenzoate sodium (E129)
Propyl hydroxybenzoate sodium
Liquid maltitol (E965)
Sodium saccharin Polysorbate 80
Citric acid anhydrous
Aniseed flavour PHL-140824
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years (unopened)

3 months (opened)

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Amber glass 100ml bottles with tamper evident child resistant HDPE cap with an EPE saranex faced liner and an adapter. The dosing device is a 5ml syringe with suitable markings which is enclosed in a cardboard carton with a PIL.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Athlone Pharmaceuticals Limited
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1 Burlington Road
Dublin 4
D04 C5Y6
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1418/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 3rd May 2024

10 DATE OF REVISION OF THE TEXT

August 2025