Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Trimoptin Tablets 100 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Trimethoprim 100 mg.
Also contains 10mg lactose monohydrate

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Flat, white, bevelled-edge tablets embossed 'TR 100'.

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.

4.2 Posology and method of administration

Trimoptin 100mg tablets are not recommended for use in children under 12 years of age. Other suitable dosage forms are available for this patient population.

1. Treatment of respiratory and urinary tract infections Adults: 200mg twice daily for 7 – 10 days

The first dosage on the first day can be doubled. Children
Over 12 years: same as adult dose
Not recommended for use in children under 12 years

2. Prophylaxis of recurrent urinary tract infection*:*

Adults: The usual dose is 100mg at night. An extra 100mg may be taken in the morning if necessary. Children
Over 12 years: same as adult dose
Not recommended for use in children under 12 years
3. Dosage in renal impairment

Creatinine Clearance (ml/sec)	Plasma creatinine (micromole/l)	Dosage advised
Over 0.45	Men <250 Women <175	Normal
0.25 - 0.45	Men 250-600 Women 175-400	Normal for 3 days then half dose
Under 0.25	Men >600 Women >400	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.

Route of administration: Oral.

4.3 Contraindications

Hypersensitivity to Trimethoprim or any of the excipients.
Severe hepatic insufficiency.
Severe renal insufficiency unless plasma levels can be monitored regularly.
Megaloblastic anaemia and other blood dyscrasias.
Trimethoprim should not be administered to premature infants or children under 6 weeks of age.
Trimoptin should not be administered to pregnant women, (See Section 4.6).
Patients with fragile X chromosome.
Patients with porphyria.

4.4 Special warnings and precautions for use

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

Trimethoprim may cause depression of haemopoiesis. Regular haematological tests should be undertaken in patients receiving long term treatment and those predisposed to folate deficiency (eg, the elderly) to check for possible pancytopaenia. 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 checked by appropriate haematological monitoring. It may be necessary to discontinue trimethoprim if this treatment is to be effective.
Particular care should be exercised in the haematological monitoring of children on long term therapy.
Patients with marked impairment of renal function: Care should be taken to avoid accumulation and resulting adverse hepatological effect. 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.

Close monitoring of serum electrolytes is advised in patients at risk of hyperkalaemia (see section 4.8).

Concomitant use of medicinal products known to cause hyperkalaemia with Trimethoprim may result in severe hyperkalaemia.

Monitoring of blood glucose is advised if co-administered with repaglinide (see section 4.5).

Elevations in serum potassium have been observed in some patients treated with trimethoprim. 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 (eg: 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).

Discontinue treatment if rash develops.

Severe cutaneous adverse reactions (SCARs)
Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with trimethoprim treatment (see section 4.8).
Patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, trimethoprim should be withdrawn immediately and an alternative treatment considered (as appropriate).
If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of trimethoprim, the treatment must not be restarted in this patient at any time.

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per 100mg tablet, 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 receiving concomitant folate antagonists or anticonvulsants.

Bone marrow depressants: Trimethoprim may increase the risk for bone marrow aplasia. Cytotoxic agents such as azathioprine, mercaptopurine and methotrexate increase the risk of haematological toxicity when given with trimethoprim.

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

Rifampicin may decrease trimethoprim concentration.

Procainamide: Trimethoprim increases plasma concentration of procainamide

Diuretics: In elderly patients concurrently taking diuretics, particularly thiazides, there is an increased incidence of thrombocytopenia with purpura. Rare cases of hyponatraemia have been reported in patients treated with trimethoprim and potassium sparing diuretics and/or thiazide diuretics. Hyperkalaemia may be exacerbated by concomitant administration of potassium sparing diuretics and/or thiazide diuretics, potassium supplements, potassium-containing salt substitutes, renin-angiotensin system inhibitors (eg: ACE inhibitors or renin angiotensin receptor blockers), other potassium increasing substances (eg: heparin) and aldosterone antagonists (eplerenone). Monitoring of potassium should be undertaken as appropriate (see section 4.4).

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

Repaglinide: Trimethoprim may enhance the hypoglycaemic effects of repaglinide. (See section 4.4)

Anticoagulants: Trimethoprim may potentiate the anticoagulant effect of warfarin and other coumarins.

Lamivudine: Trimethoprim may increase the plasma concentration of lamivudine.

ACE inhibitors: The likelihood of hyperkalaemia is increase when ACE inhibitors are taken with Trimethoprim

Amiodarone: Increased risk of ventricular arrhythmia

Oral typhoid vaccine: Inactivated by antibacterials

Potassium-sparing diuretics and aldosterone antagonists: Increased risk of hyperkalaemia

Oral contraceptive: Reports of contraceptive failure after taking trimethoprim as Trimethoprim may possibly reduce the contraceptive effect of oestrogens.

Others: Increased risk of haematological toxicity with azathioprine, methotrexate, mercaptopurine, and pyrimethamine.

Dofetilide: Serum levels increased with trimethoprim

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

An increased risk of nephrotoxicity has been reported with the use of trimethoprim and cyclosporin.

Trimoptin may interfere with diagnostic tests including serum methotrexate assay where dihydrofolate reductase is used and the Jaffe reaction for creatinine.

In addition to other medicinal products known to cause hyperkalaemia concomitant use of trimethoprim/sulfamethoxazole (co-trimoxazole) with spironolactone may result in clinically relevant hyperkalaemia.

4.6 Fertility, pregnancy and lactation

Pregnancy
Trimoptin should not be given to pregnant women, premature infants or infants during the first few weeks of life.

Epidemiological studies have shown an increased risk of spontaneous abortion and congenital malformations, in particular neural tube defects, oral clefts and cardiovascular defects, in children of mothers treated with trimethoprim during the first trimester of pregnancy. The presumed mechanism of action is thought to be interference with folates.

Breast- Feeding
Trimoptin is excreted in breast milk. This should be kept in mind when considering administration to breast feeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects of ability to drive and use machines have been performed. Trimethoprim has minor effects on the ability to drive or use machines. It may cause ataxia, syncope, uveitis or vertigo and therefore caution should be advised if a patient experiences any of these effects.

4.8 Undesirable effects

The following list of undesirable effects have been reported by health care professionals. Sometimes it may be difficult to distinguish reactions caused by the condition being treated from adverse drug reactions, which means that not all the listed reactions were caused by drug administration.

The frequencies of the undesirable effects listed below are categorised as follows:
Very common 1/10,
Common 1/100 and <1/10,
Uncommon 1/1000 and <1/100,
Rare 1/10,000 and <1/1000,
Very rare <1/10,000,
Not known: cannot be estimated from the available data.

Infections and Infestations

Common: Monilial overgrowth.
Not known: Aseptic meningitis.
Aseptic meningitis was rapidly reversible on withdrawal of the drug, but recurred in a number of cases on re-exposure to either co-trimoxazole or to Trimoptin alone.

Blood and lymphatic system disorders
Very rare: Leucopenia, neutropenia, thrombocytopenia, pancytopaenia, bone marrow depression, agranulocytosis, aplastic anaemia, haemolytic anaemia, eosinophilia, purpura, haemolysis.

Fatalities have been reported (especially in the elderly, or those with impairment of renal or hepatic function in whom careful monitoring is advised - refer to section 4.3 Contraindications), however, the majority of haematological changes are mild and reversible when treatment is stopped.
Not known: Depression of haemopoiesis (see sections 4.4).

Immune system disorders

Very rare: Drug fever, allergic vasculitis resembling Henoch-Schoenlein purpura, periarteritis nodosa, systemic lupus erythematosus.

Not known: Hypersensitivity, anaphylaxis

Metabolism and nutrition disorders Very common: Hyperkalaemia.
Very rare: Hypoglycaemia, hyponatraemia, anorexia.

Close supervision is recommended when Trimoptin is used in elderly patients or in patients taking high doses as these patients may be more susceptible to hyperkalaemia and hyponatraemia.

Psychiatric disorders

Very rare: Depression, hallucinations, confusional states, agitation, anxiety, abnormal behaviour, insomnia and nightmares.

Nervous system disorders

Common: Headache.
Very rare: Dyskinesias, tremor, ataxia, dizziness, lethargy, syncope, paraesthesiae, convulsions, peripheral neuritis, vertigo, tinnitus.

Eye disorders
Not known: Uveitis
Respiratory, thoracic and mediastinal disorders

Very rare: Cough, shortness of breath, wheeze, epistaxis.
Gastrointestinal disorders
Very rare: Constipation, glossitis, stomatitis, pseudomembranous colitis, pancreatitis.
Not known: Nausea, vomiting, gastrointestinal upset.

Hepatobiliary disorders
Very rare: Elevation of serum transaminases, elevation of bilirubin levels, disturbances of liver enzyme values, cholestatic jaundice, hepatic necrosis. Cholestatic jaundice and hepatic necrosis may be fatal.

Not known: Disturbances of liver enzyme values, jaundice

Skin and subcutaneous tissue disorders
Common: Urticaria,
Very rare: Photosensitivity, exfoliative dermatitis, fixed drug eruption, erythema multiforme, erythema nodusum, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous dermatitis, purpura.

Lyell's syndrome (toxic epidermal necrolysis) carries a high mortality.
Not known: Angioedema, Pruritus, skin rash, photosensitivity, angioedema. Erythema multiforme, Steven Johnson syndrome, toxic epidermal necrolysis, Drug reaction with eosinophilia and systemic symptoms (DRESS)
Musculoskeletal and connective tissue disorders
Very rare: Arthralgia.
Not known: Myalgia.
Renal and urinary disorders
Very rare: Impaired renal function (sometimes reported as renal failure), haematuria. Trimethoprim may affect haemopoiesis (See sections 4.4 & 4.5)

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

Treat symptomatically, gastric lavage and forced diuresis can be used.
Depression of haematopoiesis by Trimoptin can be counteracted by intramuscular injections of calcium folinate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Trimethoprim and derivatives ATC Code J01EA01
Mechanism of action
Trimethoprim is a dihydrofolate reductase inhibitor, inhibiting the conversion of bacterial dihydrofolic acid to tetrahydrofolic acid, required for the synthesis of some amino acids.
Its effects are considerably greater on the cells of micro-organisms than on the mammalian cells.

In vitro trimethoprim has effect on most Gram-positive and Gram-negative aerobic organisms, including enterobacteria such as *E Coli*, *Proteus, Klebsiella pneumoniae, Streptococcus faecalis, Streptococcus pneumoniae, Haemophilus influenzae* and *Staphylococcus aureus.*

It has no effect on *Mycobacterium tuberculosis, Neisseria gonorrhoeae, Pseudomonas aeruginosa, Treponema pallidum, Brucella abortis* or anaerobic bacteria.

Mechanisms of resistance

Resistance to trimethoprim may be due to several mechanisms. Clinical resistance is often due to plasmid mediated dihydrofolate reductases that are resistant to trimethoprim: such genes may become incorporated into the chromosome via transposons. Resistance may also be due to overproduction of dihydrofolate reductase, changes in cell permeability, or bacterial mutants which are intrinsically resistant to trimethoprim because they depend on exogenous thymidine and thymine for growth. Emergence of resistance to trimethoprim does not appear to be any higher in areas where it is used alone than in areas where trimethoprim is used in combination with sulphonamides. Nonetheless, trimethoprim resistance has been reported in many species, and very high frequencies of resistance have been seen in some developing countries, particularly among Enterobacteriaceae.

Breakpoints

EUCAST clinical MIC breakpoints to separate susceptible (S) pathogens from resistant (R) pathogens are:

EUCAST Species-related breakpoints (Susceptible/Resistant>) Units: mg/L		
Enterobacteriaceae	***Staphylococcus***	***Enterococcus***
2/ >4	2/ >4	0.032/ >1*

*The activity of trimethoprim is uncertain against enterococci. Hence the wild type population is categorized as intermediate.

Breakpoints for *S. pneumoniae* and *H. Influenzae* are not defined.

5.2 Pharmacokinetic properties

Absorption and Biotransformation
Trimoptin is readily absorbed from the gastro-intestinal tract and peak concentrations in the circulation occur about 3 hours after a dose is taken. It is bound to plasma proteins. Tissue concentrations are reported to be higher than serum concentrations with particularly high concentrations occurring in the kidneys and lungs but concentrations in the cerebrospinal fluid are about one half of those in the blood.

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

Elimination
About 40 to 50% of a dose is excreted in the urine within 24 hours mainly as unchanged drug, hence patients with impaired renal function, such as the elderly, may require a reduction in dosage due to accumulation. It appears in breastmilk. 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Povidone
Crospovidone
Sodium starch glycollate
Magnesium stearate

6.2 Incompatibilities

None applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C. Store in the original package. Protect from light.

6.5 Nature and contents of container

Polypropylene tablet container of 15, 18, 20, 21, 28, 30, 100 or 500 tablets with a high-density/low-density polyethylene blend cap and low-density polyethylene snap filler. Also available in a PVC blister with aluminum lidding foil containing 28 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Athlone Pharmaceuticals Limited
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Dublin 4
D04 C5Y6
Ireland

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

May 2026