Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Monotrim 10 mg/ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 10 mg trimethoprim.

Excipients with known effect:
Each ml of this medicine contains 408 mg sorbitol, 1.3 mg methyl parahydroxybenzoate and 0.85 mg sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension.
White, homogenous suspension with odour of aniseed and peppermint.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Monotrim 10 mg/ml Oral Suspension is indicated for the treatment of the following infections in adults and children from the age of 6 weeks (see section 5.1):

- Urinary tract infections
- Respiratory tract infections..

Monotrim 10 mg/ml Oral suspension is indicated for prophylaxis of the following infections in adults and children (see section 5.1):

- Recurrent urinary tract infections.

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

4.2 Posology and method of administration

Posology

Consult local or national prescribing guideline for antibiotic use before prescribing.

1. Treatment of respiratory and urinary tract infections:

Adults and children over 12 years: The usual dosage is 200 mg (20 ml) every 12 hours (based on dosage of 3 mg/kg body weight every 12 hours)
Maximum dose: 200 mg every 12 hours.

Paediatric population (children 6 weeks to 12 years): Based on dosage of 3 mg/kg body weight daily in two equal dosages:
6 weeks to 5 months: 25 mg (2.5 ml) every 12 hours
6 months to 3years*:* 25 mg (2.5 ml) - 50 mg (5 ml) every 12 hours
4 years to 7 years: 50 mg (5 ml) – 75 mg (7.5 ml) every 12 hours
8 years to 12 years 75 mg (7.5 ml) – 125 mg (12.5 ml) every 12 hours

Maximum dose: 4 mg/kg every 12 hours

2. Prophylaxis of recurrent urinary tract infection:

Adults and children over 12 years: The usual dose is 100 mg (10ml) at night.
Paediatric population (children under 12 years): Treatment is based on 2.5 mg/kg body weight daily given once daily as a single dose in the evening.
3. Dosage in renal impairment:

eGFR (ml/min)	Dosage advised
Over 30	normal
15-30	normal for 3 days then half dose
Under 15	half 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.

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to trimethoprim or to any of the excipients.

Pregnancy, 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. 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 or tacrolimus). If concomitant use of the above-mentioned agents is deemed appropriate, monitoring of serum potassium is recommended (see section 4.5).

Excipients
This medicine contains 2,04 g sorbitol in each 5 ml which is equivalent to 408 mg/ml.

Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

This medicine contains methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per ml oral suspension, 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.

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.

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 (eg: ACE inhibitors or renin angiotensin receptor blockers) and other potassium increasing substances (eg: heparin or tacrolimus). 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 should not be used during pregnancy.

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

4.7 Effects on ability to drive and use machines

Monotrim 10 mg/ml Oral Suspension 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.

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 such *as E. coli, Proteus, Klebsiellapneumoniae, Streptococcus faecalis, Streptococcus pneumoniae, Haemophilus influenzae*, and *Staphylococcus aureus.*

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

Mechanism 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*.
Susceptibility testing breakpoints
MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European committee on Antimicrobial Susceptibility Testing (EUCAST) for trimethoprim and are listed here: :
https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

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.

5.2 Pharmacokinetic properties

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

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. Tissue concentration is generally higher than plasma concentration.

Elimination
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 dosage.

5.3 Preclinical safety data

Not relevant (widely used in clinical practice).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carmellose sodium
Microcrystalline cellulose
Carboxymethylcellulose sodium
Ammonium glycyrrhizinate
Methyl parahydroxybenzoate (E218)
Sorbitol (E420)
Star anise oil
Peppermint oil
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
Discard any remaining solution 28 days after first opening.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Amber glass bottle with child resistant plastic closure
Pack size: 1 bottle containing 100 ml oral suspension

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Taw Pharma (Ireland) Limited
104 Lower Baggot Street
Dublin 2
Dublin
D02 Y940
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23081/014/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 April 1982

Date of last renewal: 16 April 2007

10 DATE OF REVISION OF THE TEXT

April 2026