SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Trimethoprim 100 mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Trimethoprim
Each tablets contains 100 mg Trimethoprim
Also contains lactose. For excipients see 6.1

3 PHARMACEUTICAL FORM

Tablet
Flat white tablets with bevelled edges marked MP44 on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of susceptible infections caused by Trimethoprim sensitive organisms, including most Gram-positive and Gram-negative aerobic organisms, including Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella pneumoniae, Staphylococcus aureus, E. coli, Enterobacter, Proteus and Streptococcus faecalis.

Exceptions include anaerobic bacteria. Mycobacterium tuberculosis, Neisseria gonorrhoea, Pseudomonas aeruginosa and Treponema pallidum.

Prophylaxis of recurrent urinary tract infections.

4.2 Posology and method of administration

Posology
Acute infections:
Treatment should continue for a period of between three days (e.g. uncomplicated bacterial cystitis in women) and two weeks according to the nature and severity of infection. The first dose can be doubled.
Adults and children over 12 years: 200mg twice daily.
Children 6-12 years: 100mg twice daily.
Children under 6 years of age: Not recommended; a more suitable dosage form should be used in this age group.

Elderly: Dosage is dependent upon kidney function; see special dosage schedule.
Long-term treatment and prophylactic therapy:
Adults and children over 12 years: 100mg at night.
Children 6-12 years: 50mg at night. Where a single daily dose is required, dosage at bedtime may maximise urinary concentrations. The approximate dosage in children is 2mg trimethoprim per kg body weight per day.
Elderly: Dosage is dependent upon kidney function; see special dosage schedule
Advised dosage schedule where there is reduced kidney function:

Creatinine Clearance	Plasma creatinine (micromol/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

Trimethoprim is removed by dialysis. However, it should not be administered to dialysis patients unless plasma concentrations can be estimated regularly.
Route of Administration:
For Oral Administration

4.3 Contraindications

- Trimethoprim hypersensitivity
- Severe hepatic insufficiency
- Severe renal insufficiency
- Megaloblastic anaemia and other blood dyscrasias.

Trimethoprim should not be administered to premature infants or children under 4 months of age.
Pregnancy - Trimethoprim should not be administered to pregnant women.

4.4 Special warnings and precautions for use

Patients with marked impairment of renal function; care should be taken to avoid accumulation and resulting adverse hepatological effects.
Regular haematological tests should be undertaken in patients receiving long-term treatment and those pre-disposed to folate deficiency. The elderly may be more susceptible to folate deficiency and a lower dose may be advisable.
Patients and their carers should be told how to recognize signs of blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.
Particular care should be exercised in the haematological monitoring of children on long-term therapy.

Trimethoprim should be prescribed with caution in patients with porphyria. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs affecting the immune response (e.g. azathioprine) and cytotoxic drugs (e.g. mercaptopurine) increase the risk of haematological toxicity with trimethoprim.
Trimethoprim increases antifolate effect of methotrexate (avoid concomitant use) and phenytoin. Also, increased risk of antifolate effect with pyrimethamine.
Ciclosporin may increase the risk of nephrotoxicity when given with trimethoprim.
The plasma concentration of procainamide, phenytoin and possibly digoxin and zalcitabine is increased with concomitant use of trimethoprim. Plasma concentrations of both drugs may increase when trimethoprim is given with dapsone.
Antibacterial: Rifampicin may reduce plasma concentration
Increased risk of hyperkalaemia when trimethoprim is given with eplerenone.
Trimethoprim may potentiate the anticoagulant effect of warfarin and possibly coumarins.
*Antidiabetics;*Trimethoprim rarely enhances the effects of sulphonylureas.
Trimethoprim increases hypoglycaemic effects of repaglinide when given together.
Oestrogens; antibacterials that do not induce liver enzymes possibly reduce contraceptive effects of oestrogens.

4.6 Fertility, Pregnancy and lactation

The usual caution in prescribing any drug for women of childbearing age should be exercised with Trimethoprim, Pregnancy is a contra-indication due to the teratogenic risk as Trimethoprim is a folate antagonist, especially in first trimester.
Trimethoprim is not contra-indicated for short-term use in lactating mothers, although the drug is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Gastro-intestinal disturbances including nausea and vomiting, headache, skin rashes, pruritis, urticaria, hyperkalaemia and depression of haematopoiesis have been reported occasionally.

Erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis, photosensitivity and other allergic reactions including angioedema, anaphylactic reactions and anaphylactoid reactions have been reported rarely. Aseptic meningitis has also been reported.
Cases of Megaloblastic anaemia during prolonged therapy with Trimethoprim in doses higher than those recommended rarely occur but are reversible with discontinuation of therapy and administration of folinic acid.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Trimethoprim has potent anti microbial activity through its selective inhibition of bacterial dihydrofolate reductase. It is effective against most gram-positive and gram-negative aerobic organisms.

5.2 Pharmacokinetic properties

Absorption is by the oral route. Peak plasma levels are reached in about one hour but significant plasma levels are obtained within half an hour.

Excretion is mainly in the urine in the form of unchanged drug.
Trimethoprim may cause an apparent rise in serum creatinine levels due to competition in the tubular secretory mechanisms.

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Povidone
Crospovidone
Sodium starch glycollate Type A
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months all pack sizes

6.4 Special precautions for storage

a) Containers: Do not store above 25°C. Keep the container tightly closed.
b) Blister packs: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Polypropylene or high density polystyrene with polythene closures and polyurethane wads or polythene inserts.
Pack sizes: 50, 100, 500, 1000, 5000.

250 micron PVC glass-clear/bluish rigid PVC (pharmaceuticals grade).
20 micron hard-tempered aluminium foil coated on the dull side with 6-7 gsm heat seal lacquer and printed on the bright side.
Pack sizes: 28

6.6 Special precautions for disposal and other handling

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Genethics Europe Limited
41 - 43 Klimentos
Klimentos Tower
Nicosia 1061
Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 42976/0027

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

6 October 2000

10 DATE OF REVISION OF THE TEXT

12/04/2016