SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT :

1.1 Brand Name : **L-Trim DS Tablet**
1.2 Generic Name : Trimethoprim & Sulphamethoxazole Tablets BP
1.3 Strength : Trimethoprim 160mg + Sulphamethoxazole 800mg per tablet
1.4 Pharmaceutical Form : Tablet

2. QUALITATIVE & QUANTITATIVE COMPOSITION :

Each uncoated tablet contains:

Trimethoprim	BP	160mg
Sulphamethoxazole	BP	800mg

3. PHARMACEUTICAL FORM

Tablet

White coloured, elongated, biconvex uncoated tablet, having central Breakline on one face of each tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

L-Trim DS Tablet (Co-trimoxazole) is indicated for treatment of susceptible infections, prophylaxis and trteatment of Pneumocystis jirovecii (Pneumocystis carinii) infections.

4.2 Posology and method of administration

Treatment of susceptible infections:

Child 6 weeks–5 months: 120 mg twice daily, alternatively 24 mg/kg twice daily**.**

Child 6 months–5 years: 240 mg twice daily, alternatively 24 mg/kg twice daily.

Child 6–11 years: 480 mg twice daily, alternatively 24 mg/kg twice daily.

Child 12–17 years: 960 mg twice daily.

Adult: 960 mg twice daily.

Treatment of Pneumocystis jirovecii (Pneumocystis carinii) infections (undertaken where facilities for appropriate monitoring available-consult microbiologist and product literature):

Child: 120 mg/kg daily in 2–4 divided doses for 14–21 days, oral route preferred for children

Adult: 120 mg/kg daily in 2–4 divided doses for 14–21 days.

Prophylaxis of Pneumocystis jirovecii (Pneumocystis carinii) infections:

Child: 450 mg/m2 twice daily (max. per dose 960 mg twice daily) for 3 days of the week (either consecutively or on alternate days), dose regimens may vary, consult local guidelines.

Adult: 960 mg once daily, reduced if not tolerated to 480 mg once daily, alternatively 960 mg once daily on alternate days, alternate day dose to be given 3 times weekly, alternatively 960 mg twice a day on alternate days, alternate day dose to be given 3 times weekly.

4.3 Contraindications:

It is contraindicated in patients with known hypersensitivity to sulphonamides, trimethoprim or co-trimoxazole.

4.4 Special warnings and special precautions for use:

Asthma , avoid in blood disorders (unless under specialist supervision), avoid in infants under 6 weeks (except for treatment or prophylaxis of pneumocystis pneumonia) because of the risk of kernicterus, elderly (increased risk of serious sideeffects), G6PD deficiency (risk of haemolytic anaemia), maintain adequate fluid intake, predisposition to folate deficiency & predisposition to hyperkalaemia (in adults).

4.5 Interaction with other FPPs and Other forms of Interaction

Trimethoprim & Sulfonamides increases the concentration of antiepileptics (fosphenytoin, phenytoin). Monitor and adjust dose. Pyrimethamine increases the risk of side-effects when given with Trimethoprim & Sulfonamides. Trimethoprim & Sulfonamides is predicted to increase the anticoagulant effect of coumarins. Dapsone increases the exposure to trimethoprim and trimethoprim increases the exposure to dapsone. Sulfonamides are predicted to increase the risk of methaemoglobinaemia when given with Dapsone.

Hepatic Impairment: Advised to avoid in severe liver disease.

Renal Impairment: In children: Avoid if estimated glomerular filtration rate less than 15 mL/minute/1.73m2 and if plasma sulfamethoxazole concentration cannot be monitored. In adults: Avoid if eGFR less than 15 mL/minute/1.73m2 and if plasma sulfamethoxazole concentration cannot be monitored.
Dose adjustments: In children: Use half normal dose if estimated glomerular filtration rate 15–30 mL/minute/1.73m2.
In adults: Use half normal dose if eGFR 15–30 mL/minute/1.73m2.

4.6 Pregnancy and lactation

Pregnancy: Teratogenic risk in first trimester (trimethoprim a folate antagonist). Neonatal haemolysis and methaemoglobinaemia in third trimester; fear of increased risk of kernicterus in neonates appears to be unfounded.
Lactation: Small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfamethoxazole).

4.7 Effects on ability to drive and use machines

A detrimental effect on such activities cannot be predicted from the pharmacology of the drug.

4.8 Undesirable effects

Common or very common: Diarrhoea, electrolyte imbalance, fungal overgrowth, headache, nausea, skin reactions.

Uncommon: Vomiting

Rare or very rare: Agranulocytosis, Angioedema, aplastic anaemia, appetite decreased, arthralgia, ataxia, cough, depression, dizziness, dyspnoea, eosinophilia, fever, haemolysis, haemolytic anaemia, hallucination, hepatic disorders, hypoglycaemia, leucopenia, lung infiltration, .megaloblastic anaemia, meningitis aseptic, metabolic acidosis, methaemoglobinaemia, myalgia, myocarditis allergic, nephritis tubulointerstitial, neutropenia, oral disorders, pancreatitis, peripheral neuritis, photosensitivity reaction, pseudomembranous Enterocolitis, renal impairment, renal tubular acidosis, seizure, serum sickness, severe cutaneous adverse reactions (SCARs), systemic lupus erythematosus (SLE), thrombocytopenia, tinnitus, uveitis, vasculitis, vertigo.

Side-Effects, Further Information: Co-trimoxazole is associated with rare but serious side effects. Discontinue immediately if blood disorders (including leucopenia, thrombocytopenia, megaloblastic anaemia, eosinophilia) or rash (including Stevens-Johnson syndrome or toxic epidermal necrolysis) develop.

4.9 Overdose & Treatment

Nausea, vomiting, dizziness and confusion are likely signs/ symptoms of overdosage. If vomiting has not occurred, induction of vomiting may be desirable. Gastric lavage may be useful, though absorption from the gastrointestinal tract is normally very rapid and complete within approximately two hours. This may not be the case in gross overdosage. Dependant on the status of renal function administration of fluids is recommended if urine output is low. Both trimethoprim and active sulfamethoxazole are moderately dialysable by haemodialysis. Peritoneal dialysis is not effective.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterial

Mechanism of action:

Co-trimoxazole is an antibacterial drug composed of two active principles, sulfamethoxazole and trimethoprim. Sulfamethoxazole is a competitive inhibitor of dihydropteroate synthetase enzyme. Sulfamethoxazole competitively inhibits the utilisation of para-aminobenzoic acid (PABA) in the synthesis of dihydrofolate by the bacterial cell resulting in bacteriostasis. Trimethoprim reversibly inhibits bacterial dihydrofolate reductase (DHFR), an enzyme active in the folate metabolic pathway converting dihydrofolate to tetrahydrofolate. Depending on the conditions the effect may be bactericidal. Thus trimethoprim and sulfamethoxazole block two consecutive steps in the biosynthesis of purines and therefore nucleic acids essential to many bacteria.

5.2 Pharmacokinetic properties

Absorption: After oral administration trimethoprim and sulfamethoxazole are rapidly and nearly completely absorbed. Peak levels in the blood occur between one and four hours after ingestion and the level attained is dose related.

Distribution: Approximately 50% of trimethoprim in the plasma is protein bound.

Metabolism: Renal excretion of intact sulfamethoxazole accounts for 15-30% of the dose. This drug is more extensively metabolised than trimethoprim, via acetylation, oxidation or glucuronidation. Over a 72 hour period, approximately 85% of the dose can be accounted for in the urine as unchanged drug plus the major (N4-acetylated) metabolite.

Elimination: The half-life of trimethoprim in man is in the range 8.6 to 17 hours in the presence of normal renal function.

5.3 Preclinical safety data

None Known

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

SN	Ingredients	Spec.
1	Starch (Maize)	BP
2	Sodium Methyl Hydroxybenzoate (Sodium Methylparaben)	BP
3	Sodium Propyl Hydroxybenzoate (Sodium Propylparaben)	BP
4	Gelatin	BP
5	Purified Talc (Talcum)	BP
6	Magnesium Stearate	BP
7	Colloidal Anhydrous Silica (Colloidal Silicon Dioxide)	BP
8	Sodium Starch Glycolate	BP

6.2 Incompatibilities

Not Known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Protect from light. Keep out of reach of children. Keep away from moisture. Store at a temperature not exceeding 30˚C.

6.5 Nature and contents of container

10 blisters of 10 tablets packed in an inner carton. (10 x 10)

6.6 Instructions for use and handling

Please see the package insert.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

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8. MARKETING AUTHORISATION NUMBER

06877/07821/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

a) Date of latest renewal: Feb 1, 2022

10. DATE OF REVISION OF THE TEXT

01/01/2023