

Trimethoprim (TMP)

Antibiotic Class:

Trimethoprim [2, 4-diamino-5- (3', 4', 5'-trimethoxybenzyl) pyrimidine] is a diaminopyrimidine.

Antimicrobial Spectrum:

Streptococcus pyogenes, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Listeria monocytogenes*, *Escherichia coli*, *Shigella dysenteriae*, *Salmonella typhi*, *Salmonella enteritidis*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Proteus mirabilis*, *Haemophilus influenzae*, *Pasteurella multocida*, *Bordetella pertussis*. Trimethoprim also has activity against *Pneumocystis carinii*, *Toxoplasma gondii*, *Plasmodium falciparum*.

Mechanism of Action:

Trimethoprim inhibits thymidine and DNA synthesis.

Pharmacodynamics

No data

Pharmacokinetics:

C_{max}: 1-2mcg/mL; Half-life: 10-12; Volume of distribution: 100-120 L; Table 7

Trimethoprim is rapidly absorbed following oral administration with a high bioavailability.

Approximately 44% of trimethoprim is bound to plasma proteins. Trimethoprim achieves high concentrations in breast milk.

Adverse Effects:

GI – nausea, vomiting

Hematologic – pancytopenia, agranulocytosis, macrocytic anemia, thrombocytopenia

Skin – toxic erythema, erythema nodosum, fixed local eruption, erythema multiforme, Lyell's syndrome, Exfoliative dermatitis, urticaria, necrotizing vasculitis, photodermatitis, toxic erythema

Renal – transient blood urea and creatinine elevations, crystalluria, acute interstitial nephritis

CNS – headache, confusion, depression, aseptic meningitis

Dosage:

Oral: 100mg and 200mg tablets

50mg/5ml suspension

Dosing in adults:

Urinary tract infection: 100mg PO q12h or 200mg PO q24h x 10 days

Dosing in children:

Acute otitis media: (=6 months old) 10mg/kg suspension divided PO q12h x 10 days

Disease state based dosing:

Renal failure: CrCl 15-30 mL/min, 50 mg every 12 hr; CrCl less than 15 mL/min, not recommended

Hepatic failure: No dosage adjustment necessary.

Contraindications/Warnings/Precautions:

Contraindications: megaloblastic anemia due to folate deficiency

Precautions: patients with possible folate deficiency, impaired renal function

Drug Interactions:

Other diaminopyrimidines-pyrimethamine, azathioprine, or methotrexate are potentiated by TMP, resulting in severe leucopenia.

Pregnancy:

Category C. Trimethoprim interferes with folate metabolism.

Monitoring Requirements:

Therapeutic: Monitor signs and symptoms of infection. Monitor white blood cell count, culture and susceptibility

Toxic: Monitor renal function tests, serum potassium.

Brand names/Manufacturer: Proloprim®/Allergan, Primsol/Medicis pharmaceuticals, Trimplex/Roche pharmaceuticals