

Trimethoprim (TMP) Sulfamethoxazole (SMX)

Antibiotic Class:

Antibiotic (trimethoprim and sulfonamide combination in a 5:1 ratio)

Antimicrobial Spectrum:

Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Listeria monocytogenes, Nocardia asteroides, Mycobacterium fortuitum, Escherichia coli, Shigella dysenteriae, Salmonella typhi, Salmonella enteritidis, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Stenotrophomonas maltophilia, Haemophilus influenzae, Pasteurella multocida, Bordetella pertussis, Brucella melitensis, Neisseria gonorrhoeae, Neisseria meningitides

Mechanism of Action:

Sulfamethoxazole inhibits the synthesis of dihydrofolic acid. Trimethoprim inhibits thymidine and DNA synthesis. These two agents act synergistically in inhibiting folic acid synthesis.

Pharmacodynamics

No data.

Pharmacokinetics:

Cmax: 1-2mcg/mL (TMP); 25-60mcg/mL (SMX); Half-life: 10-12 hours (TMP and SMX); Volume of distribution: 100-120 L (TMP); 12-18 L (SMX); [Table 7](#)

Adverse Effects:

GI – nausea, vomiting

Hematologic – pancytopenia, agranulocytosis, 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

Electrolytes – Hyperkalemia (higher doses)

Increased risk of adverse effects in the elderly

Dosage:

Dosage: The 1:5 ratio (TMP:SMX) remains constant in all dosage forms

Oral: Tablets Single strength (SS: 80mg/400mg TMP/SMX)

Double strength (DS: 160mg/800mg TMP/SMX)

Liquid (suspension) 40mg / 200mg TMP/SMX per 5ml

Parenteral: Vial 5ml: Single strength (80mg/400mg TMP/SMX)

10ml: Double strength (160mg/800mg TMP/SMX)

30ml: Six times strength (480mg/2400mg TMP/SMX)

Dosing in adults

Acute exacerbation of chronic bronchitis: 1 DS TMP/SMX PO q12h×14days
Pneumocystis carinii pneumonia: 2 DS TMP/SMX PO/IV q6h×14-21days
Pneumocystis carinii prophylaxis: 1DS TMP/SMX PO daily
Pulmonary nocardiosis: 160 mg/800mg TMP/SMX IV q6h or 2 DS TMP/SMX PO q12h
Traveler's diarrhea: 1DS TMP/SMX PO q12h×5days
Uncomplicated cystitis in women: 1DS TMP/SMX PO q12h×3 or 1~2DS PO×1 dose
Urinary tract infection (other):1 DS TMP/SMX PO q12h×10-14days
Stenotrophomonas infections: 2 DS TMP/SMX IV q12h
Staphylococcus aureus cellulitis: 1-2 DS TMP/SMX PO q12h×10-14days
Staphylococcus aureus osteomyelitis: 2 DS TMP/SMX PO q12h

Dosing in children

Urinary Tract Infections (10 days duration) or Middle Ear Infections (5 days duration)
The recommended dosage for children 2 months of age or older, given every 12 hours, is determined by weight.

10kg (22 pounds), 1 teaspoonful (5 ml)
20kg (44 pounds), 2 teaspoonfuls (10 ml) or 1 SS tablet
30kg (66 pounds), 3 teaspoonfuls (15 ml) or 1.5SS tablet
40kg (88 pounds), 4 teaspoonfuls (20 ml) or 2 SS or 1 DS tablet

Pneumocystis Carinii Pneumonia

The recommended doses, taken every 6 hours for 14 to 21 days, are determined by weight. Liquid (suspension) formulation 40mg/200mg TMP/SMX per 5ml

8.2kg (18 pounds), 1 teaspoonful (5 ml)
16kg (35 pounds), 2 teaspoonfuls (10 ml) or 1 SS tablet
24.1kg (53 pounds), 3 teaspoonfuls (15 ml) or 1.5 SS tablet
32.3kg (70 pounds), 4 teaspoonfuls (20 ml) or 2 SS or 1 DS tablet

Pneumocystis Carinii Pneumonia prophylaxis

The dose is determined by body surface area. The dose is given twice a day, on 3 consecutive days per week. The total dose should not exceed TMP/SMX = 320mg /1600mg. The safety of repeated use of TMP/SMX in children under 2 years of age has not been established.

Disease state based dosing:

Renal failure: CrCl < 30 mL/min: half of the usual daily dose should be administered

CrCl < 15 mL/min: TMP serum levels may be monitored

Hemodialysis: Metabolites of TMP and SMX may accumulate. Half of the maintenance dose is recommended to be administered after hemodialysis

Hepatic failure: No dosage adjustment necessary.

Contraindications/Warnings/Precautions:

Contraindications: Pregnant patients at term, nursing mothers, megaloblastic anemia due to folate deficiency

Precautions: should not be used to treat group A beta-hemolytic strep infections, patients with possible folate deficiency, severe allergies, asthma, or glucose-6-phosphate dehydrogenase deficiency, elderly patients, AIDS patients; increased risk for severe side-effects

Drug Interactions:

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

Sulfonamides displace warfarin from binding albumin, thus increasing its serum level.

SMX inhibits the clearance of phenytoin, prolonging its half-life.

Pregnancy:

Category C: Risk unknown. Human studies inadequate.

Monitoring Requirements:

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

Toxic: Monitor renal function tests, serum potassium.

Brand names/Manufacturer: Bactrim®/Roche; Septra®/GlaxoSmithKline; Sulfatrim®/Alpharma