

Trimethoprim (TMP) Sulfamethoxazole (SMX)

Antibiotic Class:

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

Antimicrobial Spectrum:

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

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

Exhibits time-dependent bactericidal activity

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

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

CNS – headache, confusion, depression, aseptic meningitis

Electrolytes – Hyperkalemia (increased risk with higher doses, in patients with renal insufficiency, and/or receiving potassium sparing diuretics, ACE inhibitors, or ARBs)

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 jirovecii pneumonia: 2 DS TMP/SMX PO/IV q6h×14-21days

Pneumocystis jirovecii 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 days

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

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 jirovecii 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 jirovecii 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 necrotizing group A beta-hemolytic strep infections, patients with possible folate deficiency, severe allergies, asthma, or glucose-6-phosphate

dehydrogenase deficiency, elderly patients. Persons with AIDS; have a higher risk for leukopenia and rash.

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 /Aspen Pharmacare; Sulfatrim/Alpharma; Co-trimoxazole/Sandoz; available as generic