Trimethoprim (TMP) Sulfamethoxazole (SMX)

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

**Antimicrobial Spectrum:**

**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: 80/mg/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 leucopenia 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