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 asteroids, 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 agents together are synergistic.

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)

Dosage:
Oral: Single strength (80mg/400mg TMP/SMX), Double strength (160mg/800mg TMP/SMX) tablets; TMP 40mg/5mL and SMX 200mg/5mL oral suspension
IV: TMP 16mg/mL and SMX 80mg/mL solution for injection

Dosing in adults:
Acute exacerbation of chronic bronchitis - 160mg/800mg TMP/SMX PO q12h x 14 days
Pneumocystis carinii pneumonia: 15-20 mg/kg TMP component/day PO/IV divided q6h x 14-21 days
Traveler's diarrhea: 160mg/800mg TMP/SMX PO q12h x 5 days
Uncomplicated cystitis in women: 160mg/800mg TMP/SMX PO q12h x 3 OR 160mg/800mg to 320mg/1600mg PO x 1 dose

Urinary tract infection (other): 160mg/800mg TMP/SMX PO q12h x 10-14 days
Stenotrophomonas infections: 5mg/kg TMP component IV q12h

Dosing in children:
Otitis media: (=2 months of age) 8 mg/kg TMP component/day divided PO every 12h x10 days
Urinary tract infectious disease: (=2 months of age) 8 mg/kg TMP component/day divided PO q12h x 10 days

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