Trimethoprim/Sulfamethoxazole (TMP/SMX)

SPECTRUM OF ACTIVITY

- **Gram-positive organisms:** *S. aureus* (including most methicillin-resistant *S. aureus*) and coagulase-negative staphylococci. Also effective against *Listeria monocytogenes* and some *Nocardia spp.*
- **Gram-negative organisms:** many *E. coli, Proteus spp., Klebsiella spp.*, *Stenotrophomonas maltophilia* and SPICE organisms
- **Fungal and parasitic organisms:** *Pneumocystis jirovecii* and *Toxoplasma gondii*

INDICATION AND DOSAGE

- TMP/SMX has good oral bioavailability and tissue penetration (e.g. CNS, bone, soft tissues, lung)
- TMP/SMX can be used in staphylococcal skin and soft tissue infections, but should not be used as monotherapy for non-purulent cellulitis due to intrinsic streptococcal resistance
- Dose adjustment required for patients with severe renal insufficiency (CrCl < 30mL/min), consult pharmacist
- IV to PO conversion: 10mL of IV solution = 1 Double Strength (DS) tablet = 160 mg TMP/800 mg SMX

Syndrome	Organism	Weight-based Dosing[a]	Typical Dosing[b,c]
Skin/Soft Tissue Infection			
Purulent	*S. aureus*	5 mg/kg/day in 2 divided doses	1 DS tablet PO BID
Pneumonia			
	P. jirovecii	15-20 mg/kg/day in 3-4 divided doses	2 DS tablets PO TID
	Enterobacteriaceae	5-10 mg/kg/day in 2 divided doses	2 DS tablets PO BID
	Stenotrophomonas	10-15 mg/kg/day in 3 divided doses	2 DS tablets PO TID
Cystitis/Pyelonephritis			
	Enterobacteriaceae	5 mg/kg/day in 2 divided doses	1 DS tablet PO BID
Central Nervous System Infection			
	T. gondii	10 mg/kg/day in 2 divided doses	2 DS tablets PO BID
	L. monocytogenes	15-20 mg/kg/day in 3-4 divided doses	2 DS tablets PO QID

[a] Dose expressed in mg/kg of trimethoprim (TMP) per day

[b] Assuming normal renal function and 70 kg dosing weight. For conversion to IV therapy, see "Indications and Dosage"

[c] Dosing intervals between BID-QID can be used to reduce per dose tablet quantity as required

CONTRAINDICATIONS/PRECAUTIONS

- **TMP/SMX use requires close monitoring (including *after* hospital discharge) especially in the elderly, those on prolonged treatment, patients with diabetes, renal dysfunction, or haematological diseases.**
- Safety issues include renal failure, hyperkalemia, myelosuppression, and drug interactions in older patients and those with chronic medical conditions.
- TMP/SMX should not be used
  - in cases of known hypersensitivity or severe drug reaction to TMP/SMX
  - in patients with G-6-PD deficiency due to risk of hemolysis
  - during the 1st and late 3rd trimesters of pregnancy
  - to treat severe infections due to *S. aureus*
  - to treat infections caused by streptococci (e.g. non-purulent cellulitis) or enterococci
- Significant risk for drug interactions (e.g. warfarin, angiotensin converting enzyme-inhibitors, angiotensin II receptor blockers, aldosterone antagonists, sulfonylureas [e.g. glyburide, glicazide]), consult a pharmacist

ADVERSE DRUG REACTIONS

- Rash, including Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, is rare (~4.3 cases/million users in one week) but significantly more common than other antimicrobials (8-30 times higher incidence).
- Hyperkalemia, hypoglycemia and renal dysfunction may occur and are more likely in higher doses and/or in those with pre-existent renal dysfunction, advanced age or other medical comorbidity
- Bone marrow toxicity with resultant thrombocytopenia is rare but possible
- Regular monitoring of CBC, potassium and SCr should be performed while on therapy

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REFERENCES

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