

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	<i>S. aureus</i>	5 mg/kg/day in 2 divided doses	1 DS tablet PO BID
Pneumonia			
	<i>P. jirovecii</i>	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
	<i>Stenotrophomonas</i>	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			
	<i>T. gondii</i>	10 mg/kg/day in 2 divided doses	2 DS tablets PO BID
	<i>L. monocytogenes</i>	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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