



TMP-SMX vs. *Streptococcus* spp.

Skin and soft tissue infections are typically categorized as either purulent or [non-purulent](#). The most common causative pathogen in purulent skin and soft tissue infections is *Staphylococcus aureus*, whereas the most common causative pathogens in non-purulent skin and soft tissue infections is beta-hemolytic *Streptococcus* spp. (Group A/B/C/G streptococcus). In clinical situations where activity against both is desired, [trimethoprim-sulfamethoxazole \(TMP-SMX\)](#) and a beta-lactam is recommended to treat *S. aureus*, including methicillin-resistant *S. aureus* (MRSA), and beta-hemolytic *Streptococcus* spp., respectively.¹ However, is the beta-lactam really needed?

Does TMP-SMX have activity against beta-hemolytic streptococcus?

Yes, but TMP-SMX was thought to be inactive against beta-hemolytic streptococcus for a long time, explaining recommendations to combine it with a beta-lactam to cover for streptococcus causing non-purulent cellulitis. This belief stemmed from flawed microbiology practices where culture medium used in susceptibility testing contained high thymidine concentrations. Thymidine inhibits TMP-SMX, resulting in false resistance. Contemporary culture medium has low levels of thymidine. In a recent study, TMP-SMX was found to be active against 85 different beta-hemolytic streptococcus isolates. Specific species included *S. pyogenes* (n=49), *S. agalactiae* (n=20), and *S. dysgalactiae* (n=16).²

Does clinical data support TMP-SMX efficacy in non-purulent cellulitis?

Yes, oral TMP-SMX (85%) was found to be non-inferior to intramuscular penicillin (85%) in the treatment of impetigo in children.³ In another randomized controlled trial, no differences in clinical cure were seen between clindamycin and TMP-SMX in patients with uncomplicated skin infections including cellulitis only, abscess only, and mixed cellulitis and abscesses.⁴

Key Takeaways: TMP-SMX monotherapy can be used to treat skin infections where *S. aureus* (including MRSA) and beta-hemolytic *Streptococcus* spp. are a concern. The addition of a beta-lactam to cover for streptococcus is not needed.

References:

1. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014 Jul 15;59(2):e10-52.
2. Cho C, Shields RK, Kline EG, et al. In vitro activity of clindamycin, doxycycline, and trimethoprim/sulfamethoxazole against clinical isolates of β -hemolytic *Streptococcus* spp. via BD Phoenix and broth microdilution. *Antimicrob Steward Healthc Epidemiol*. 2023;3(1):e238. Published 2023 Dec 15. doi:10.1017/ash.2023.515
3. Bowen AC, Tong SY, Andrews RM, et al. Short-course oral co-trimoxazole versus intramuscular benzathine benzylpenicillin for impetigo in a highly endemic region: an open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2014;384(9960):2132-2140. doi:10.1016/S0140-6736(14)60841-2
4. Miller LG, Daum RS, Creech CB, et al. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. *N Engl J Med*. 2015;372(12):1093-1103. doi:10.1056/NEJMoa1403789