# Warfarin + Sulfamethoxazole-trimethoprim

Sulfamethoxazole-trimethoprim (SMZ-TMP) is a sulfonamide antibiotic that may potentiate the anticoagulant effects of warfarin, resulting in an increased INR and risk of bleeding. The mechanism of the interaction seems to be multifactorial by altering normal flora (reducing vitamin K synthesis), protein binding site displacement, and reducing warfarin metabolism through the cytochrome P450 isozyme 2C9. Increased INR monitoring and warfarin dose adjustments may be necessary to reduce the risk of serious bleeding, if suitable antibiotic substitution is not available.

| Is there a suitable alternative antibiotic for this indication? | Yes | No | | |
|---|---|---|---|---|
| Is the patient a candidate for preemptive warfarin dose reduction? | | Yes | No | |
| Is the patient >65 years old? | | | Yes | No |
| Use alternative antibiotic with a low-risk profile | ■[1] | | | |
| Consider warfarin dose reduction prior to initiating SMZ-TMP and increased INR monitoring | | ■[2] | | |
| Increased risk of bleeding | | | ◆[3] | ■[2] |

○ = No special precautions. ■ = Assess risk and take action if necessary. □◆ = Use only if benefit outweighs risk

**Footnotes**:

1. Cephalexin, clindamycin, and levofloxacin seem to have a lower risk profile that may not necessitate a warfarin dose adjustment, but increased INR monitoring is recommended. (Lane et al. Am J Med. 2014; 127(7):657-663) (Ahmed et al. J Thromb Thrombolysis. 2008; 26(1):44-8)
2. If warfarin and sulfamethoxazole-trimethoprim are co-administered, a prophylactic warfarin dose reduction of 10-25% with increased INR monitoring and subsequent dose adjustments is recommended. (Ahmed et al. J Thromb Thrombolysis. 2008; 26(1):44-8) (Powers et al. J Thromb Thrombolysis. 2017; 44:88-93)
3. Older patients taking warfarin may have an increased risk of bleeding when SMZ-TMP is initiated. (Baillargeon et al. Am J Med. 2012; 125(2):183-189) (Fischer et al. Arch Intern Med. 2010; 170(7):617-621)

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