## 3 Venous Thromboembolism /Urinary tract infection

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Recommendations for Venous Thromboembolism (VTE) prescribe treatment with DOACs[[1]](#footnote-1) as preferred line of treatment, or warfarin, which may be indicated in other cases[[2]](#footnote-2). For bacterial urinary tract infection (UTI), guidelines recommend treatment with an antibiotic such as trimethoprim–sulfamethoxazole (TMP/SMX) because of its low cost, effectiveness and familiarity among clinicians. The primary mechanisms by which antibiotic medications interact with warfarin to increase the risk of major bleeding is through disruption of intestinal flora that synthesize vitamin K, and inhibition of cytochrome p450 isozymes which metabolize warfarin[[3]](#footnote-3). Interactions between warfarin and specific antibiotic agents have been widely assessed, also for the specific case of UTI[[4]](#footnote-4). The antibiotics most likely to interfere with warfarin are TMP/SMX, ciprofloxacin, levofloxacin, metronidazole, fluconazole, azithromycin, and clarithromycin. Low-risk agents include clindamycin, cephalexin, and penicillin G3. Notwithstanding, concomitant treatment with warfarin and TMP/SMX is still considered an effective management option for VTE/UTI comorbidity, as long as the risk of bleeding, as indicated by the International Normalized Ratio (INR), is carefully monitored2. When the risk of bleeding increases, the warfarin dose has to be reduced to compensate; once INR values return to normal, the original warfarin dose should be reinstated.

**Patient case**: Sixty-seven-year-old female on a long-term anticoagulation therapy (warfarin due to financial considerations) because of recurrent VTE.

**Current problem**: Recurrent VTE

**Current medication**: warfarin (5mg/day)

**New problem**: UTI

**Management scenario**: Patient presents with the symptoms of a strong and persistent urge to frequently urinate and describes experiencing burning sensation when urinating. A preliminary diagnosis of the cystitis UTI is confirmed by lab results. Considering that for last episode of the UTI, she was prescribed TMP/SMX (Bactrim, 1 double-strength tablet orally, twice daily for at least 3 days) and it was well-tolerated, similar treatment for current episode of the cystitis UTI was followed[[5]](#footnote-5).

**Adverse interactions and revisions**: Because of the interactions between warfarin and TMP/SMX, a pre-emptive reduction of 10% of warfarin dosage is recommended[[6]](#footnote-6). Considering her total weekly warfarin dose is 35 mg, her reduced daily dose becomes 4.5 mg per day (calculated as (35 – 3.5)/7 = 4.5).

Beginning on day 3 of therapy, INRs should be measured daily and warfarin doses adjusted to achieve an INR >= 2.0 as soon after day 5 of overlapping therapy as possible[[7]](#footnote-7).

**Revised treatment for VTE and UTI**: warfarin (4.5mg/day), bactrim (2 double-strength tablet/day for at least 3 days). Re-evaluate starting on day 3 of overlapping therapy depending on the INR value.

1. Wells, G. et al. Direct Oral Anticoagulants For The Treatment Of Venous Thromboembolic Events. University of Ottawa. 2016. See p. 9, highlighted. [↑](#footnote-ref-1)
2. Witt, D. M. et al. Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. J Thromb Thrombolysis. 2016; 41:187–205. See p. 1, p. 3-5 (highlighted). [↑](#footnote-ref-2)
3. Onysko M, Holcomb N, Hornecker J. Antibiotic interactions: Answers to 4 common questions. The Journal of Family Practice. 2016; 65(7): 442-448. See p. 1, 2 (highlighted) [↑](#footnote-ref-3)
4. Fischer HD. et al. Hemorrhage during warfarin therapy associated with cotrimoxazole and other urinary tract anti-infective agents. Archives of Internal Medicine. 2010;170:617–21. See p. 1 (highlighted) [↑](#footnote-ref-4)
5. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women, p. 3 (highlighted) [↑](#footnote-ref-5)
6. Ahmed A, Stephens JC, Kaus CA, et al. Impact of preemptive warfarin dose reduction on anticoagulation after initiation of trimethoprim-sulfamethoxazole or levofloxacin. Journal of Thrombosis and Thrombolysis. 2008;26:44-48. See p. 1 (highlighted) [↑](#footnote-ref-6)
7. Witt, D. M. et al. Guidance for the practical management of warfarin therapy. J Thromb Thrombolysis. 2016; 41:187–205. See p. 5 (highlighted). [↑](#footnote-ref-7)