

Safety of Combination Treatment with Tranexamic Acid (TXA) and Combined Hormonal Contraceptives (CHCs) for Reducing Menstrual Blood Loss

TXA and CHCs (oral pills, patches, etc.) are often prescribed together because they are effective for the treatment of heavy menstrual bleeding or abnormal uterine bleeding. CHCs reduce blood loss by up to 40-50% and TXA reduces it by 40-59% from baseline.¹ CHCs are generally used continuously throughout a menstrual cycle whereas TXA is used intermittently on days of heavy bleeding.

Some interaction checkers may flag this combination of CHCs and TXA as contraindicated due to an increased risk of thrombotic events, but **TXA's role in increasing risk of venous thromboembolism is controversial.**²

The US product monograph includes a history of VTE or elevated risk of thrombosis (including current use of CHCs) as a contraindication.^{2,3} The Canadian product monograph suggests avoiding the combination of TXA and CHCs if the risk of a thrombotic event outweighs the benefit of medical treatment.⁴

TXA is anti-fibrinolytic and it stops bleeding by preventing the breakdown of clots already formed.^{1,5,6} Studies have not confirmed a significantly elevated risk of thrombosis with TXA use.

- A small retrospective study that looked at women with risk factors for VTE did not find an elevated risk of VTE among this population when antifibrinolytics were administered.⁷
- A cohort study following around 2 million women in Denmark found VTE and arterial thrombosis to be very rare adverse effects of treatment with TXA. The number needed to harm for VTE per five days of treatment was 78,549 people.⁸
- A randomized, double-blind, placebo-controlled trial (WOMAN) reviewed the use of TXA in postpartum hemorrhage and did not find a statistically significant increase in the risk of thromboembolic events (pulmonary embolism, deep-vein thrombosis, myocardial infarction, and stroke) in the TXA group versus placebo. People in the postpartum period are at high risk of thromboembolic events.⁶
- A 2018 literature review on the use of TXA in heavy menstrual bleeding reported on clinical experience (particularly in Sweden, where TXA is available over-the-counter) and concluded that that the benefit of TXA, even when combined with combined hormonal contraceptives, will outweigh risks for most women. The authors did note that women with increased risks for VTE (immobility, obesity, coagulopathy, etc.) should probably avoid combination therapy.⁹

A patient-specific assessment of benefit and risk is important to consider when you encounter prescriptions for both agents for a patient. Both therapies are effective and can be safely used together to reduce menstrual blood loss during a menstrual cycle in those who do not have additional risk factors for VTE.

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References:

- ACOG committee opinion no. 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol. 2013 Apr;121(4):891-896. doi: 10.1097/01.AOG.0000428646.67925.9a.
- Kaunitz A. Abnormal uterine bleeding in nonpregnant reproductive-age patients: management. UpToDate. Wolters Kluwer. Updated August 29, 2023. Accessed September 12, 2023. <u>https://www.uptodate.com/contents/abnormal-uterine-bleeding-in-nonpregnant-reproductive-age-patients-management</u>
- Tranexamic acid. In: *Lexicomp.* Wolters Kluwer. Updated September 19, 2023. Accessed September 19, 2023. <u>https://online-lexi-</u> com.cyber.usask.ca/lco/action/doc/retrieve/docid/patch_f/7798
- 4. Cyklokapron. Product Monograph. Pfizer Canada ULC; 2021. Accessed September 12, 2023. https://pdf.hres.ca/dpd_pm/00063720.PDF
- Singh S, Best C, Dunn S, Leyland N, Wolfman WL. No. 292-Abnormal Uterine Bleeding in Pre-Menopausal Women. J Obstet Gynaecol Can. 2018 May;40(5):e391-e415. doi: 10.1016/j.jogc.2018.03.007.
- WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. The Lancet. 2017 May 27;389(10084):2105-16. doi: 10.1016/S0140-6736(17)30638-4.
- 7. Lindoff C, Rybo G, Åstedt B. Treatment with Tranexamic Acid during Pregnancy, and the Risk of Thrombo-Embolic Complications. Thrombosis and Haemostasis. 1993;70(02):238–40.
- 8. Meaidi A, Mørch L, Torp-Pedersen C, Lidegaard O. Oral tranexamic acid and thrombosis risk in women. EClinicalMedicine. 2021 May 6;35:100882. doi: 10.1016/j.eclinm.2021.100882.
- Thorne J, James P, Reid R. Heavy menstrual bleeding: is tranexamic acid a safe adjunct to combined hormonal contraception? Contraception. 2018 Jul;98(1):1-3. doi: 10.1016/j.contraception.2018.02.008.

For more reading on this topic:

 Relke N, Chornenki NLJ, Sholzberg M. Tranexamic acid evidence and controversies: An illustrated review. Res Pract Thromb Haemost. 2021 Jul 14;5(5):e12546. doi: 10.1002/rth2.12546. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8279901/</u>