

Ref. N°: DD/PVCT/2765/FDA/2025

## SAFETY INFORMATION COMMUNICATION

Medical Product category	Title
Warfarin and Tramadol	Risk of drug interactions leading to severe bleeding

### 1. Introduction

Reference is made to the law N° 003/20218 of 09/02/2018 establishing Rwanda FDA, and to the regulations governing pharmaceutical products and medical devices, especially Article 23 on safety information and communication.

Reference is made to the WHO Pharmaceutical Newsletter, which has reminded healthcare professionals that taking warfarin and tramadol together can cause harmful drug interactions, which in some patients could be fatal.<sup>1</sup>

Warfarin is a vitamin K antagonist (VKA) oral anticoagulant (OAC) commonly prescribed to prevent stroke, venous thromboembolism (VTE), and other thromboembolic complications in patients with atrial fibrillation and mechanical heart valves. Warfarin is primarily used with other medications, such as Tramadol. Combining these drugs can significantly increase the International Normalized Ratio (INR), a measure of blood clotting, which can lead to severe bruising, bleeding, and even fatal outcomes.<sup>2,4</sup>

It is against this background that Rwanda FDA communicates these important risks to healthcare professionals and patients for the adoption of adequate risk minimization measures.

### 2. Information to the Patients and Caregivers

- Patient should be aware that warfarin can interact with some medicines, such as tramadol, leading to an increased risk of bleeding.
- Patient are recommended to seek medical treatment and have an urgent International Normalised Ratio test if they experience any of the following symptoms:
  - a. Prolonged nose bleeds (more than 10 minutes)
  - b. Blood in vomit, sputum (phlegm), stool (poo) or urine (pee)
  - c. Severe or unexplained bruising
  - d. Severe bleeding gums
  - e. Unusual headaches (headaches with blurred vision, slurred speech, loss of movement, feeling or being sick, fits, loss of consciousness, dizziness)
  - f. Women who experience heavy or increased bleeding during their menstrual period or any other heavy vaginal bleeding

- Patients should inform the healthcare professional that they are taking warfarin.
- Patients should not take any new medicines without discussing with their healthcare professional.
- Patients should not stop taking warfarin without discussing with the healthcare professional.
- Patients should always report suspected adverse drug reactions to the Rwanda FDA.

### 3. *Information to Healthcare Professionals*

- Healthcare Professionals should be aware that warfarin is a coumarin-derived vitamin K antagonist which has a low therapeutic index, so it is important to exercise with caution when co-prescribing warfarin with other drugs like Tramadol, to minimise the risk of drug interactions.
- Healthcare Professionals should be aware of the risk of increased INR when warfarin and tramadol are used together, with a risk of major bruising and bleeding, which could be life-threatening.
- Healthcare Professionals should take caution if tramadol is co-prescribed with other coumarin-derived anticoagulants.
- Healthcare Professionals should consider whether additional monitoring of INR is required when starting tramadol or another concomitant medicine.
- Healthcare Professionals should ask patients about all the medicines that they are currently taking while taking warfarin.
- Healthcare Professionals should consult the product information of any new concomitant therapy for specific guidance on the use of warfarin and consider whether warfarin dose adjustment is required.
- Healthcare Professionals should ensure patients are aware of the need to seek medical treatment once they notice the signs of a major bleeding event.
- Healthcare Professionals should report suspected adverse drug reactions to the regulatory Authority.

### 4. *Information for the Marketing Authorization Holders/Manufacturers*

Marketing Authorization Holders should submit an updated SmPC for warfarin to include the risk of drug–drug interactions that may occur when warfarin and tramadol are used concomitantly. This information should be reflected in Section 4.4 (Warnings and Precautions) and Section 4.5 (Interaction with Other Medicinal Products and Other Forms of Interaction).

### 5. *Reporting channel*

Patients and Healthcare Professionals are urged to report any suspected adverse drug event/reaction associated with Warfarin and Tramadol or any other medical product to the Rwanda FDA by using an online reporting tool called VigiMobile for medicines, which is available on Rwanda FDA website at <https://vigiflow-eforms.who-umc.org/rw/adr> or using online reporting system (PVIMS) accessible on <https://pvims.rwandafda.gov.rw/security/landing>.

Sincerely,




**Prof. Emile BIENVENU**

**Director General**

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## 6. References

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2. Wang M, Zeraatkar D, Obeda M, Lee M, Garcia C, Nguyen L, et al. Drug–drug interactions with warfarin: A systematic review and meta-analysis. *Br J Clin Pharmacol*. 2021;87(11):4051–100.
3. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2 SUPPL.):e419S-e496S.
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