



بنقدم بثقة  
Moving Forward  
with Confidence



## Circular No. 101 /2024

12 -01-1446 H

18-07-2024

To:

Director General of Royal Hospital  
Director General of Khoula Hospital  
Director General of Medical Supplies (MOH)  
Director General of Pvt. Health Est. Affairs (to kindly arrange distribution to all Pvt. Health Institutions)  
Director General of Health Services in all Governorates  
Hospital Director (Al Nahda Hospital)  
Hospital Director (Al Massara Hospital)  
The Head of Medical Services in SQU Hospital  
The Head of Medical Services in Royal Oman Police  
The Head of Medical Services in Ministry of Defense  
The Head of Medical Services in The Diwan  
The Head of Medical Services in The Sultan's Special Force  
The Head of Medical Services in Internal Security Services  
The Head of Medical Services in Petroleum  
The Head of Medical Services in LNG Oman  
Director of Pharmacy of Qaboos Comprehensive Cancer Care & Research Center  
Director of Pharmacy & Medical Stores in all Governorate (for distribution pls.)  
Marketing Authorization Holders & Pharmaceutical Companies  
**ALL PRIVATE PHARMACIES & DRUG STORES**

After Compliments,

Please find attached our Circular No. 101 dated 18/07/2024 regarding:

**Drug Safety Communication:** *Warfarin and the Risk of Drug Interactions with Tramadol*

Copy to:

- Director, Office of H.E. The Undersecretary for Health Affairs
- Director of Pharmacovigilance & Drug Information Dept, DGPA&DC
- Director of Drug Control Department, DGPA&DC
- Director of Pharmaceutical Licensing Department, DGPA&DC
- Director of Central Quality Control Lab., DGPA&DC
- Section Head PV for Herbal Medicine & Health Products.
- Section Head PV for Human Medicine
- Section Head of Central Drug Information



**DSC**  
مركز سلامة الدواء  
Drug Safety Center



ص.ب: ٣٩٣ مسقط - الرمز البريدي: ١٠٠ - هاتف: ٢٢٣٥٧١١١ - فاكس: ٢٢٣٥٨٤٨٩

P.O. Box: 393 Muscat - Postal Code: 100 - Tel: 22357111 - Fax: 22358489

✉ @DSCPHO Email: dscpho@moh.gov.om



## Drug Safety Communication

### *Warfarin and the Risk of Drug Interactions with Tramadol*

<b>Drug Name and Safety Issue</b>	Warfarin: Be Alert to the Risk of Drug Interactions with Tramadol
<b>Source</b>	Medicines & Healthcare products Regulatory Agency (MHRA-UK)
<b>Summary of the Safety Issue</b>	Taking warfarin and tramadol together can cause harmful drug interactions, which can raise the International Normalised Ratio (INR) and result in severe bruising and bleeding, potentially fatal in some patients.
<b>Drug (s) Information</b>	<b>Warfarin:</b> <ul style="list-style-type: none"><li>• A coumarin-derived vitamin K antagonist used for prevention and treatment of blood clots. It is used to prevent embolisation in rheumatic heart disease and, atrial fibrillation and after insertion of prosthetic heart valves. Warfarin is also used in the prevention and treatment of venous thrombosis and pulmonary embolism and treatment of transient ischaemic attacks.</li><li>• Has a low therapeutic index, which means care is required when taking co-prescribed medicines due to the possibility of interactions that could lead to an increased risk of bleeding.</li><li>• The product information for warfarin advises that healthcare professionals should refer to the product information of any new concomitant medicines for specific guidance on use with warfarin and whether a dose adjustment or therapeutic monitoring is required. The product information will be updated to include the interaction in due course.</li></ul> <b>Tramadol</b> <ul style="list-style-type: none"><li>• A non-selective opioid analgesic, which acts as an agonist at the mu, delta and kappa opioid receptors</li><li>• The tramadol Summary of Product Characteristics (SmPC) states that caution is advised when co-administering tramadol and coumarin derivatives ( e.g. warfarin), as increased INR values with major bleeding and ecchymoses have been observed in some patients</li></ul>
<b>Details of the Safety Issue</b>	<b><u>Description of the Issue:</u></b> Concurrent use of warfarin and tramadol may lead to elevated INR levels, increasing the risk of severe bruising and bleeding. <b><u>Evidence and Data:</u></b> <ul style="list-style-type: none"><li>• A Coroner's report following the death of a patient due to a brain bleed associated with concurrent warfarin and tramadol treatment.</li></ul>



	<ul style="list-style-type: none"><li>• Reports of increased INR and major bleeding from tramadol's SmPC.</li></ul> <p><b><u>Affected Populations:</u></b> Patients on warfarin, especially those with additional risk factors for bleeding.</p>
<b>Recommendations for Healthcare Professionals</b>	<p><b><u>Monitoring and Reporting:</u></b></p> <ul style="list-style-type: none"><li>• Exercise caution when co-prescribing warfarin with other drugs.</li><li>• Monitor patients for signs of increased INR and major bleeding.</li><li>• Report suspected adverse drug reactions to Department of Pharmacovigilance &amp; Drug Information (DPV&amp;DI)</li></ul> <p><b><u>Patient Management:</u></b></p> <ul style="list-style-type: none"><li>• Ask patients about all current medications.</li><li>• Be aware of the increased risk of major bruising and bleeding when warfarin and tramadol are used together.</li><li>• Adjust warfarin dosage as necessary based on new concomitant therapy.</li><li>• Consider additional INR monitoring when starting tramadol or other new medications.</li><li>• Educate patients to seek medical treatment if they notice signs of major bleeding.</li></ul> <p><b><u>Prescribing Information:</u></b></p> <ul style="list-style-type: none"><li>• Refer to the product information for any new concomitant therapy for specific guidance on use with warfarin.</li></ul>
<b>Recommendations for Patients</b>	<p><b><u>Risk Information:</u></b></p> <ul style="list-style-type: none"><li>• Warfarin can interact with medications such as tramadol, increasing the risk of bleeding.</li></ul> <p><b><u>Action Steps:</u></b></p> <ul style="list-style-type: none"><li>• Seek medical treatment and have an urgent INR test if experiencing symptoms like prolonged nose bleeds, blood in vomit, sputum, stool, or urine, severe or unexplained bruising, severe bleeding gums, unusual headaches, or heavy vaginal bleeding.</li><li>• Inform your healthcare professional about all the medicines you are taking and carry your anticoagulant alert card at all times.</li><li>• Do not take new medications or stop taking warfarin without discussing it with your healthcare professional.</li><li>• Report suspected adverse drug reactions to the DPV&amp;DI.</li></ul>
<b>Regulatory Actions</b>	The product information for warfarin will be updated to include the interaction with tramadol.



<b>Additional Information &amp; Resources</b>	<b>References:</b> <ul style="list-style-type: none"><li>• Coroner's report on the fatal interaction between warfarin and tramadol.</li><li>• Tramadol Summary of Product Characteristics (SmPC).</li></ul> <b>Links to Resources:</b> <p><u>Warfarin: be alert to the risk of drug interactions with tramadol - GOV.UK (www.gov.uk)</u></p>
Reporting suspected ADR (s)	Please continue to report suspected adverse drug reactions (ADRs) to the Department of Pharmacovigilance & Drug Information in DSC. Reporting suspected ADRs, even those known to occur, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines. Healthcare professionals, patients, and caregivers are asked to submit reports electronically using: 1. For Drugs: <a href="https://vigiflow-eforms.who-umc.org/om/mohadr">https://vigiflow-eforms.who-umc.org/om/mohadr</a> 2. For Vaccines: <a href="https://vigiflow-eforms.who-umc.org/om/mohvac">https://vigiflow-eforms.who-umc.org/om/mohvac</a>

Dr. Mohammed Hamdan Al Rubaie  
Director General

