



SAFETY ALERT

DRAP SAFETY ALERT NO. 37

Safety Alert of Risk of Kidney Damage with Oral Anticoagulants.

Date: 20th of October, 2023.

Target Audience:

- Manufacturers and importers of oral anticoagulants;
- Healthcare professionals; and
- Patients, consumers or caregivers.

Background:

The Therapeutic Goods Administration (TGA) of Australia in June 2023 announced that a warning about serious kidney damage has been added to the prescribing information for all oral anticoagulants given through the oral route. Anticoagulant-related nephropathy (ARN) is a rare but serious adverse event resulting from profuse glomerular bleeding and has the potential to cause irreversible kidney damage and death. The TGA investigated the safety signal based on reports of ARN in patients taking oral anticoagulants, mainly from overseas and sought a piece of advice from the Advisory Committee on Medicines (ACM). The committee noted that this adverse event is now well documented in the medical literature with warfarin and there is growing evidence for other oral anticoagulants. The ACM supported a class-wide warning being added to the Product Information for all oral anticoagulants. *The ACM does not consider a warning for parenteral anticoagulants to be needed at this stage.* This is because they are mainly used in hospitals and for a shorter duration.

Action in Pakistan:

The case was discussed in the 3rd meeting of PRAEC, held on the 8th of September, 2023, which decided as per Rule 10(1)(h)(iv) of the Pharmacovigilance Rules, 2022 that registration holders should include information about Anticoagulant-related nephropathy (ARN) and its monitoring and evaluation in the warning and precaution section and to list ARN as an adverse drug reaction of unknown frequency in the prescribing information/label for oral anticoagulants.





Therapeutic Goods Affected.

Name: Oral anticoagulants are widely used to prevent and treat thromboembolic conditions and include apixaban, rivaroxaban and warfarin etc. Anticoagulants, sometimes called blood thinners, reduce the blood's natural ability to clot. *This alert does not apply to parenteral anticoagulants.*

Advice for patients.

If you are taking an oral anticoagulant and have any questions or concerns about your treatment, speak to your doctor. Do not stop taking these medicines without discussing it with your doctor first. Contact your doctor immediately if you experience any of the following signs and symptoms: high blood pressure; decreased amount of urine; blood in urine; and swelling in legs, ankles, and around the eyes, which may indicate your kidneys aren't working properly.

Advice for healthcare professionals.

Healthcare professionals are informed that early detection and intervention of ARN is critical to reducing permanent kidney damage and death. Although anticoagulant-related nephropathy is rare, it is likely underdiagnosed as kidney biopsy is required for a definitive diagnosis but is rarely performed in people taking anticoagulants, and patients who develop ARN have comorbidities that may explain their acute kidney injury presentation. Therefore, healthcare professionals are advised that while treating patients who are taking oral anticoagulants, talk to them about the risk of anticoagulant-related nephropathy. Close monitoring, including renal testing, is recommended for those with excessive anticoagulation (or supratherapeutic INR for those on warfarin) and haematuria.

Guidelines for reporting Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with oral anticoagulants (apixaban, rivaroxaban and warfarin) to the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP) through the [Med Vigilance E-Reporting System](#) available on the DRAP website. Similarly, ADRs can also be reported through Med Safety App which is available for download from the [App Store](#) (for iOS devices) and [Google Play](#) (for Android devices).





References:

- [Minutes of 3rd meeting of Pharmacovigilance Risk Assessment Expert Committee.](#)
- [TGA: Oral Anticoagulants Can Cause Serious Kidney Damage in Rare circumstances.](#)
- [TGA: Risk Of Kidney Damage with Oral Anticoagulants.](#)

