SAFETY ALERT

DRAP SAFTEY ALERT NO. 41

Safety Alert of Risk of Tendon Disorders with Third-Generation Aromatase inhibitors

Date: 20th of October, 2023.

Target Audience:

- Manufacturers and importers of third-generation aromatase inhibitors (anastrozole, exemestane and letrozole);
- Healthcare professionals; and
- Patients, consumers or caregivers.

Background:

Health Canada in January, 2023 announced that the product safety information for third-generation aromatase inhibitors (anastrozole, exemestane and letrozole) will be updated to include the risk of tendon disorders. The review was triggered by an update including the risks of tendonitis and tendon rupture by the EMA to letrozole product safety information. It was informed that Health Canada is working with the manufacturers of third-generation aromatase inhibitors to update the Candian Product Monographs to include these risks. Tendon disorders include tendon inflammation (tendonitis), inflammation of the tendon sheath (tenosynovitis) and tendon tears (tendon rupture).

Health Canada reviewed reports of events of tendonitis and tenosynovitis and their potential relation to tendon rupture in five randomized controlled trials (RCTs). The agency also reviewed 25 case reports (2 domestic and 23 international) of tendon rupture (10 cases) and tendonitis (15 cases), where a link between the risk of tendon rupture and tendonitis with the use of a third-generation aromatase inhibitor could not be ruled out. However, these case reports included other medications and/or conditions that could have contributed to the reported adverse events. The review concluded that there is likely a link between the use of third-generation aromatase inhibitors and the risks of tendonitis and tenosynovitis. Also, a link with tendon rupture could not be ruled out.

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 Pharmacovigilance Rules, 2022 that registration holders of third-generation aromatase inhibitors (anastrozole, exemestane and letrozole) should update their prescribing information by including information about tendon disorders (tendonitis, tendon rupture and tenosynovitis etc.) in the warning and precaution section and list these in adverse drugs reaction section.

Therapeutic Goods Affected.

Name: Third-generation aromatase inhibitors (**anastrozole, exemestane and letrozole**) are prescription drugs authorized for the treatment of breast cancer in women who have reached menopause (post-menopausal breast cancer).

Advice for patients.

Patients are advised to promptly notify their healthcare professional if they experience symptoms such as pain, swelling and difficulty moving their joints while they are on treatment with third-generation aromatase inhibitors (anastrozole, exemestane and letrozole).

Advice for healthcare professionals.

The use of third-generation aromatase inhibitors was found to be associated with tendonitis and tenosynovitis as reported in randomized controlled trials. Tendon rupture was found to be a potential risk. Tendonitis and tenosynovitis were estimated to be of uncommon occurrence, and tendon rupture was of rare occurrence. Treating physicians should monitor patients for these adverse drug reactions.

Guidelines for reporting Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with third-generation aromatase inhibitors (anastrozole, exemestane and letrozole) 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.
- Health Canada: Summary Safety Review - Third Generation Aromatase Inhibitors (anastrozole, exemestane, letrozole) - Assessing the Potential Risk of Tendon Disorders.