SFDA SAFETY SIGNAL

"A signal is defined by the SFDA as reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually m ore than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. A signal is a hypothesis together with data and arguments and it is important to note that a signal is not only uncertain but also preliminary in nature"

26-06-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Tacrolimus and the Risk of Bronchiectasis

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Bronchiectasis** associated with the use of **Tacrolimus**. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

Introduction

Tacrolimus capsules are indicated for the prophylaxis of organ rejection, in adult patients receiving allogeneic kidney transplant, liver transplant or heart transplant and pediatric patients receiving allogeneic liver transplants in combination with other immunosuppressants. Tacrolimus inhibit T-lymphocyte activation and proliferation, as well as T-helper-cell-dependent B-cell response (i.e., immunosuppression). [1] Bronchiectasis is a long-term condition where the airways of the lungs become widened, leading to a build-up of excess mucus that can make the lungs more vulnerable to infection. The damage caused to the lungs by bronchiectasis is permanent, but treatment can help relieve symptoms and stop the damage getting worse. [2] The aim of this review is to evaluate the risk of Bronchiectasis associated with the use of Tacrolimus and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at SFDA performed a signal review using National Pharmacovigilance Center (NPC) database, and World Health Organization (WHO) database, VigiBase, with literature screening to retrieve all related information to assess the causality between Bronchiectasis and Tacrolimus use. The search conducted on March 2025.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 38 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve global cases. [3] Authors also applied WHO-UMC causality assessment criteria on all the extracted ICSRs. [4] Among the reported cases, five were assessed as probably or possibly related to Tacrolimus, 32 cases could not be evaluated due to insufficient information, and one case was deemed unlikely to be related.

Datamining: The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values

indicates less statistical association. The IC result is (2.3) for this drug/ADR combination which reflects positive statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Tacrolimus. The search showed a published article that generally describes pulmonary injury associated with Tacrolimus use. [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Tacrolimus and Bronchiectasis. Health care professionals and health regulators must be aware of the potential risk in drug recipients.

Report Adverse Drug Events (ADRs) to the SFDA

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug reactions (ADRs) resulted from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance Center (NPC)
Saudi Food and Drug Authority-Drug sector
4904 northern ring branch rd
Hittin District
Riyadh 13513 – 7148
Kingdom of Saudi Arabia
Toll free number: 19999
Email: NPC.Drug@sfda.gov.sa

References:

1- Dailymed.nlm.nih.gov. (n.d.). DailyMed - TACROLIMUS capsule. [online] Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=bd447ffa-9196-4c3c-accf-5adf29b84665

2- NHS (2019). Overview - Bronchiectasis. [online] NHS. Available at: https://www.nhs.uk/conditions/bronchiectasis/

3- Vigilyze.who-umc.org. 2025. [online] Available at: https://vigilyze.who-umc.org/ .

4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at https://www.who.int/publications/m/item/WHO-causality-assessment .

5- Koike, R., Tanaka, M., Komano, Y., Sakai, F., Sugiyama, H., Toshihiro Nanki, Ide, H., Satoshi Jodo, Katayama, K., Matsushima, H., Miwa, Y., Morita, K., Nakashima, H., Nakamura, H., Masamitsu Natsumeda, Sato, Y., Seitaro Semba, Tateishi, M., Nobuyuki Miyasaka and Masayoshi Harigai (2011). Tacrolimus-induced pulmonary injury in rheumatoid arthritis patients. Pulmonary Pharmacology & Therapeutics, 24(4), pp.401–406. doi:https://doi.org/10.1016/j.pupt.2011.01.016