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"

29-09-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Adalimumab and the Risk of Antiphospholipid syndrome

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

Introduction

Adalimumab is a fully human, recombinant monoclonal antibody with high affinity and was the third tumor necrosis factor-alpha (TNF-α) inhibitor. Adalimumab is used to treat various autoimmune conditions such as rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, Crohn disease, and ulcerative colitis. [1] Antiphospholipid syndrome (APS) is an autoimmune disease that can cause blood clots and pregnancy complications. Most people with APS need to take blood thinners to prevent future blood clots and miscarriages. [2] The aim of this review is to evaluate the risk of Antiphospholipid syndrome associated with the use of Adalimumab 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 Antiphospholipid syndrome and Adalimumab use. The search conducted on July 2025.

Results

Cases 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 64 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 the extracted ICSRs with completeness score 0.8 and above (9 cases). [4] Of the nine cases reviewed, four were considered possibly associated with Adalimumab, while the remaining five could not be assessed due to insufficient information.

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 (1.2) for this drug/ADR combination which reflects positive statistical association. [4]

Literature: A literature search was performed by the signal team to explore potential associations between this ADR and Adalimumab. The search retrieved three publications reporting this risk in relation to Adalimumab. [5-7]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Adalimumab and Antiphospholipid syndrome. 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:

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

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5- Hemmati, I., & Kur, J. (2013). Adalimumab-associated antiphospholipid syndrome: a case report and review of the literature. Clinical rheumatology, 32, 1095-1098.

6- Cheemalavagu, S., McCoy, S. S., & Knight, J. S. (2020). Digital ischaemia secondary to adalimumab-induced antiphospholipid syndrome. BMJ Case Reports CP, 13(2), e232907.

7- Uehara, M., Matsushita, S., Aochi, S., & Yamamoto, M. (2023). Positive antiphospholipid antibodies and pulmonary embolism in a patient with adalimumab-induced lupus. Modern Rheumatology Case Reports, 7(1), 68-73.