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 more 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"

04-03-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Adalimumab and the Risk of Acute Febrile Neutrophilic Dermatosis

The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of ***Acute febrile neutrophilic dermatosis*** *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, high-affinity, recombinant anti-tumor necrosis factor (TNF) alpha monoclonal antibody used to treat rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, etc. [1] Sweet syndrome (acute febrile neutrophilic dermatosis) is a neutrophilic dermatosis characterized by the abrupt appearance of edematous and erythematous papules, plaques, or nodules on the skin. Fever, leukocytosis, and internal organ involvement can also occur. Sweet syndrome has been associated with infection, malignancy, pregnancy, and drug exposure. [2] The aim of this review is to evaluate the risk of Acute febrile neutrophilic dermatosis 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 Acute febrile neutrophilic dermatosis and Adalimumab use. The search conducted on January 2024.

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 58 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. [3] Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score 0.6 and above (n=15). [4] Among them, 7 cases of Acute febrile neutrophilic dermatosis were possibly linked to Adalimumab, 5 were not assessable due to lack of important information and finally only 3 case assessed as unlikely.

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 (0.8) 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 adalimumab. The search resulted in two reported cases of Acute febrile neutrophilic dermatosis following the use of adalimumab [5,6]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis, and literature are sufficient to suggest causal association between Adalimumab and Acute febrile neutrophilic dermatosis. 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- Ellis, C.R. and Azmat, C.E. (2022) Adalimumab, National Center for Biotechnology Information. Available at: https://pubmed.ncbi.nlm.nih.gov/32491812/ [Accessed: 03/01/2024].

2- Merola, J.F.(2022) Sweet syndrome (acute febrile neutrophilic dermatosis): Management and prognosis, UpToDate. Available at: https://www.uptodate.com/contents/sweet-syndrome-acute-febrile-neutrophilic-dermatosis-management-and-prognosis [Accessed: 03/01/2024].

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 03/01/2024].

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 [Accessed: 03/01/2024].

5- Chang YC, Yang HJ. Successful management of tumor necrosis factor-alpha inhibitor-induced Sweet syndrome in a patient with ulcerative colitis: A case report. Int J Clin Pharmacol Ther. 2022 Jan;60(1):46-51. doi: 10.5414/CP204088. PMID: 34647866.

6- Alsaleh, Anas MD2; Glover, Sarah DO1; Alkhasawneh, Ahmad MD1. Sweet's Syndrome in Crohn's Disease Patient after Treatment with Humira®: 1280. American Journal of Gastroenterology 107():p S508-S509, October 2012.