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"

05-08-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Allopurinol and the Risk of Acute generalised exanthematous pustulosis

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

Introduction

Allopurinol, a xanthine oxidase inhibitor, is a urate-lowering medication that is approved for managing gout, preventing tumor lysis syndrome, and preventing recurrent calcium nephrolithiasis in patients with hyperuricosuria. [1] Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous adverse reaction in which tiny nonfollicular sterile pustules with underlying erythema develop and spread rapidly. Most cases of AGEP occur as an adverse drug reaction, but cases have also been reported following infectious insults or contact with physical triggers. [2] The aim of this review is to evaluate the risk of Acute generalised exanthematous pustulosis associated with the use of Allopurinol 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 generalised exanthematous pustulosis and Allopurinol use. The search conducted on May 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 97 global case-reports while only single local case found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs with compeleteness score of 0.81 and above (n=34 cases). [4] Among them, one case assessed as certain causality, 28 cases were probably and possibly linked to Allopurinol, and 3 cases assessed as not assessable due to lack of essential information, while the remaining 2 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 (3.3) for this drug/ADR combination which reflects strong positive statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Allopurinol. The search showed one published case-report of Acute generalised exanthematous pustulosis following the use of Allopurinol [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis, and literature are suggestive for causal association between Allopurinol and Acute generalised exanthematous pustulosis. Health care professionals and health regulators must be aware of this 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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2- Moore MJ, Sathe NC, Ganipisetti VM. Acute Generalized Exanthematous Pustulosis. [Updated 2023 May 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK592407/ [Accessed: 26/05/2024].

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3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 27/05/2024].

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: 27/05/2024].

5- Lun, K., & Harley, W. (2002). Allopurinol-induced pustular eruption: an unusually mild case. Australasian journal of dermatology, 43(2), 140-143. [Accessed: 27/05/2024].