

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”

01-03-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Lactulose and the Risk of Pruritus

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

Introduction

Lactulose is a synthetic sugar used to treat constipation. It is broken down in the colon into products that pull water out from the body and into the colon. This water softens stools. Lactulose is also used to reduce the amount of ammonia in the blood of patients with liver disease. It works by drawing ammonia from the blood into the colon where it is removed from the body. ^[1] Pruritus, or itching, is a frequent complaint heard by dermatologists and primary care physicians. Although generally considered a benign symptom, pruritus can have adverse effects on a patient’s wellbeing and can be incapacitating when severe. The mechanisms of pruritus are not particularly well understood and are compounded by the subjective nature of the process itself. Pruritus occurs with a host of dermatological conditions, but can also be a marker of systemic disease. Dermatologists and primary care physicians must be aware of the varied causes of itching. ^[2] The aim of this review is to evaluate the risk of Pruritus associated with the use of Lactulose 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 Pruritus and Lactulose use. The search conducted on February 2023.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The Saudi national database resulted in one reported local case. The WHO database resulted in 340 global case-reports. The author selected top 30 cases with completeness score of 1.0 for further analysis. ^[3] Authors also applied WHO-UMC causality

assessment criteria on the 30 ICSRs, which resulted in most of them possibly linked to Lactulose (14 probable + 11 possible + 5 unlikely = 30 ICSRs).^[4]

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, considering the null value equal to zero. The results of (IC= 0.2) revealed a slightly positive statistical association for the drug/ADR combination.^[3]

Conclusion

The weighted cumulative evidence identified from assessed local and global cases are sufficient to suggest causal association between Lactulose and Pruritus. 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@sfd.gov.sa

References:

- 1- MedlinePlus.gov (2017). lactulose page. Available at: <https://medlineplus.gov/druginfo/meds/a682338.html>
- 2- Tivoli, Y. A., & Rubenstein, R. M. (2009). Pruritus: An updated look at an old problem. The Journal of clinical and aesthetic dermatology, 2(7), 30.
- 3- Vigilyze.who-umc.org. 2023. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed 28/02/2023].
- 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 28/02/2023].