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"

21-11-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Rivaroxaban and the Risk of Pemphigoid

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

Introduction

Rivaroxaban is a selective inhibitor of FXa. It inhibits free FXa and prothrombinase activity. Rivaroxaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin. By inhibiting FXa, rivaroxaban decreases thrombin generation. [1] Bullous pemphigoid is a rare skin condition that causes large, fluid-filled blisters. They develop on areas of skin that often flex such as the lower abdomen, upper thighs or armpits. Bullous pemphigoid is most common in older adults. [2] The aim of this review is to evaluate the risk of Pemphigoid associated with the use of Rivaroxaban 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 Pemphigoid and Rivaroxaban use. The search conducted on October 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 WHO database resulted in 52 global case-reports. [3] The authors applied WHO-UMC causality assessment criteria on the 12 ICSRs of compeleteness score of 0.8 and above, which resulted in more than half of them are either possibly or probably linked to Rivaroxaban (3 probable + 5 possible + 2 not assessable +2 unlikely = 12 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= 0.7) revealed a positive statistical association for the drug/ADR combination. [3]

Literature: On October 4th 2023, the author searched for eligible publications. As a result two published case report found supportive for this signal. [5,6]

Conclusion

The weighted cumulative evidence identified from assessed cases, literature and data mining are sufficient to suggest causal association between Rivaroxaban and Pemphigoid. 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 - Xarelto- rivaroxaban tablet, film coated (no date) U.S. National Library of Medicine. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=38b11f5d-f0fc-46dc-aef1-ea31872bb621 (Accessed: 08 October 2023).
2- Bullous pemphigoid (2022) Mayo Clinic. Available at: https://www.mayoclinic.org/diseases-conditions/bullous-pemphigoid/symptoms-causes/syc-20350414#:~:text=Bullous%20pemphigoid%20(BUL%2Dus%20PEM,abdomen%2C%20upper%20thighs%20or%20armpits. (Accessed: 08 October 2023).
3- Vigilyze.who-umc.org. 2023. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 07/08/2023].
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 07/08/2023].
5- Liang, J. (Calvin) et al. (2021) 'Rivaroxaban-associated bullous pemphigoid in a patient with atrial fibrillation', CJC Open, 3(10), pp. 1316–1319. doi:10.1016/j.cjco.2021.06.003.
6- Valencia López, R. et al. (2020) 'Penfigoide Ampolloso Asociado Al Uso de Rivaroxaban', Acta Médica Grupo Ángeles, 18(4), pp. 422–423. doi:10.35366/97272.