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"

06-03-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Dabigatran and the Risk of Acute Kidney Injury

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

Introduction

Dabigatran etexilate is an oral prodrug of dabigatran, a direct thrombin inhibitor that provides the first available oral anticoagulant alternative to warfarin for reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AF). [1] Acute kidney injury, previously known as acute renal failure, denotes a sudden and often reversible reduction in the kidney function, as measured by increased creatinine or decreased urine volume.[2] The aim of this review is to evaluate the risk of Acute Kidney Injury associated with the use of Dabigatran 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 Kidney Injury and Dabigatran 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 1602 global case-reports while the national Saudi database resulted in one local case. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. [3] Authors also applied WHO-UMC causality assessment criteria on top 30 ICSRs with completeness score of 1.0 (n=30). [4] Among them, 24 cases of Acute Kidney Injury were possibly linked to Dabigatran, one case were not assessable due to lack of important information and finally only five 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 (2.3) 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 our drug of interest. The search showed two published case-reports of Acute Kidney Injury associated with the use of Dabigatran [5,6]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis, global regulatory and literature are sufficient to suggest causal association between Dabigatran and Acute Kidney Injury. 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- Sarah, S. (2013). The pharmacology and therapeutic use of dabigatran etexilate. The Journal of Clinical Pharmacology, 53(1), 1-13.

2- Goyal, A., Daneshpajouhnejad, P., Hashmi, M. F., & Bashir, K. (2017). Acute kidney injury.

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 16/01/2024].

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: 16/01/2024].

5- Li, X., & Cheung, C. Y. (2019). Dabigatran causing severe acute kidney injury in a patient with liver cirrhosis. CEN Case Reports, 8, 125-127.

6- Novak, J. E., Alamiri, K., & Yee, J. (2018). Dabigatran reversal in a patient with end-stage liver disease and acute kidney injury. American Journal of Kidney Diseases, 71(1), 137-141.