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"

24-03-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Bisoprolol and the Risk of Hyperkalaemia

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

Introduction

Bisoprolol is a medication used to manage and treat hypertension and congestive heart failure. The drug belongs to the selective beta-blocker class of drugs and acts explicitly as a cardioselective beta1-blocker (B1-blocker). [1] Hyperkalemia occurs when renal potassium excretion is limited by reductions in glomerular filtration rate, tubular flow, distal sodium delivery or the expression of aldosterone-sensitive ion transporters in the distal nephron. [2] The aim of this review is to evaluate the risk of Hyperkalaemia associated with the use of Bisoprolol 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 Hyperkalaemia and Bisoprolol use. The search conducted on February 2024.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). In Saudi Arabia, the number of local cases that reported (Hyperkalaemia) in association with the use of (Bisoprolol) is 103 cases. Most of the ICSRs were female 72.8% while 27.2% were male. The seriousness criteria showed non-serious conditions are 96.1% and the rest were serious 3.9%. Most of the cases reported in 2021 (68.9%) followed by 2022 (30.1%) and only (1%) reported in 2020. Globally, the WHO database resulted in 278 global case-reports (387 including the Saudi Cases). 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 top completeness score 1.0 (n=30). [4] Among them, 24 cases of Hyperkalaemia were probably or

possibly linked to the this medication, 6 case assessed as unlikely and finally 2 cases were not assessable due to lack of important information.

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 (3.7) 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 Bisoprolol. The search showed an article mentioning this risk in association with beta blockers class [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis, and literature are sufficient to suggest causal association between Bisoprolol and Hyperkalaemia. 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- Bazroon, A. A., & Alrashidi, N. F. (2023). Bisoprolol. In StatPearls. StatPearls Publishing. [Accessed: 25/2/2024].

2- Hunter, R. W., & Bailey, M. A. (2019). Hyperkalemia: pathophysiology, risk factors and consequences. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 34(Suppl 3), iii2–iii11. https://doi.org/10.1093/ndt/gfz206 [Accessed: 03/01/2024].

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 25/2/2024].

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: 25/2/2024].

5- Kassem, H., Hajjar, C., El Gharbi, T., & Turner, L. (2009). Hyperkaliémie secondaire à la prise d'aténolol. La Revue de médecine interne, 30(8), 714-716.