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"

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Saudi Food and Drug Authority (SFDA) – Safety Signal of Agomelatine and the Risk of Hypertension

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

Introduction Agomelatine is antidepressant drugs, which is agonist at melatonin MT1 and MT2 receptors and as a neutral antagonist at 5-HT2C receptors [1]. Agomelatine is indicated to treat major depressive episodes in adults. [2]. Hypertension or high blood pressure is a common condition in which the long-term force of the blood against artery walls is high enough that it may eventually cause health problems, such as heart disease [3]. The aim of this review is to evaluate the risk of Hypertension associated with the use of Agomelatine and to suggest regulatory recommendations if required.

Methodology Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between Agomelatine and the Risk of Hypertension [4] We used the WHO-Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [5]

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 47 global ICSRs as of November 29th 2020 [4]. The reviewers have selected and assessed the causality for the well-documented ICSRs with completeness scores of 0.7 and above (19 ICSRs); the value 1.0 indicated the highest score for best-written ICSRs. Among the reviewed cases, about more than half of them provides supportive association (3 probable, and 9 possible cases). Also, there are 13 positive dechallenges and 5 positive rechallenges.

Data Mining: 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, which means " blood pressure increase" with "Agomelatine" have been observed slightly more than expected when compared to other medications available in WHO database [4].

Pharmacological Plausibility: In a report available on WHO signal detection tool (vigilyze) have mentioned that, melatonin which is structurally closely related to agomelatine is known to cause hypertension. Melatonin binds to the MT receptors and is used for sleep disorders such as short-term primary insomnia or to decrease jet lag. In European medicine Agency (EMA), hypertension is labeled as adverse drug reaction that appeared following the use of melatonin [6].

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, data mining, WHO signal assessment report are sufficient to support a causal association between Agomelatine and the risk of Hypertension. Health regulators and health care professionals must be aware for this potential risk and shall monitor any signs or symptoms in treated patients.

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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6. WHO Signal reports (2020) of Agomelatine and blood pressure increase. Vigilyze database: Available at: https://www.dec.gov.ua/wp-content/uploads/farmakonaglyad/EMA/2020/Agomelatine_and_Increased_Blood_Pressure.pdf#:~:text=Twenty%2Dfour%20reports%20have%20been,(BPI)%20under%20agomelatine%20treatment.&text=On%2014%20April%202019%2C%2024,agomelatine%20administration%20(Table%201).