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"

21-1-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Indapamide and the Risk of Rhabdomyolysis

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

Introduction Indapamide appears to cause vasodilation, probably by inhibiting the passage of calcium and other ions (sodium, potassium) across membranes it is indicated to treat hypertension, treatment of salt and fluid retention associated with congestive heart failure [1, 2]. Rhabdomyolysis is a syndrome characterized by muscle necrosis and the release of intracellular muscle constituents into the circulation [3]. The aim of this review is to evaluate the risk of Drug reaction with Rhabdomyolysis and the associated with the use of Indapamide 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 causal relationship between Indapamide and the Risk of Rhabdomyolysis [4].WHO-Uppsala Monitoring Centre (UMC) criteria used as standard for assessing the causality of the reported cases [5]

Results

Case Review: The number of resulted cases for the reported drug/adverse drug reaction are 33 global ICSRs as of August 23, 2020. The ICSR's with completeness score ›0.7 (n=10); Among the 10 reviewed cases, seven cases with positive dechallenge, and the application of the WHO causality assessment yielded four cases with probable association and five with possible association, and one unassessable case.

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= 1.1) revealed a positive statistical association for the drug/ADR combination, which means

"Rhabdomyolysis" with the use of "Indapamide" have been observed more than expected when compared to other medications available in WHO database [4].

Additional Evidence: The WHO initiated investigation aimed to assess the causality and the possible risk factors for Rhabdomyolysis reported with the use of Indapamide. The results suggest that Rhabdomyolysis can occur as consequence of severe hypokalemia induced by Indapamide, considering that as plausible mechanism for the ADR [6].

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, data mining and the WHO investigation are sufficient to support a causal association between Indapamide and the risk of Rhabdomyolysis. Health regulators and health care professionals must be aware of this potential risk and it is advisable to 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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2. DrugBank (2020). Indapamide - DrugBank. Available at: https://www.drugbank.ca/drugs/DB00808 [Accessed 8/23/2020].
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4. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org [Accessed 10/4/2020].
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6. Uppsala Monitoring Centre. Indapamide-induced (acute hypokalaemic) rhabdomyolysis. Available at: https://www.who-umc.org/media/165201/indapamide-inducedfinalweb.pdf [Accessed 9/6/2020]