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 Etoposide and Risk of Electrolyte imbalance

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

Introduction

Etoposide and teniposide are semisynthetic analogues of podophyllotoxin that are used as antineoplastic agents in the therapy of several forms of solid tumors, leukemia and lymphoma, usually in combination with other agents. Both etoposide and teniposide are associated with an appreciable rate of serum enzyme elevations during therapy, and high doses have been implicated in causing clinically apparent acute liver injury including sinusoidal obstruction syndrome. [1] Electrolytes are essential for basic life functioning, such as maintaining electrical neutrality in cells, generating and conducting action potentials in the nerves and muscles. Sodium, potassium, and chloride are the significant electrolytes along with magnesium, calcium, phosphate, and bicarbonates. Electrolytes come from food and fluids. These electrolytes can have an imbalance, leading to either high or low levels. High or low levels of electrolytes disrupt normal bodily functions and can lead to even life-threatening complications. [2] The aim of this review is to evaluate the risk of electrolytes imbalance associated with the use of Etoposide 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 Etoposide and the risk of Electrolytes imbalance. [3][4] WHO-Uppsala Monitoring Centre (UMC) criteria have been used as standard for assessing the causality of the reported cases. [5]

Results

Case Review: The search in the Saudi vigilance database resulted in two cases (Hyperkalemia and Hypokalemia). One of the cases has been assessed as possible causal association while the other was

not assessable. [3] The search in the World Health Organization (WHO) database (Vigibase) resulted in 88 cases. [4] The author selected cases with completeness score of 0.8 and above for further analysis (ICSRs=8). The causality assessment resulted in five possible cases, one unlikely case and two cases were unassessable.

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 result of (IC= 2.4) revealed a positive statistical association for the drug/ADR combination, which means "Electrolytes imbalance" with the use of "Etoposide" have been observed more than expected when compared to other medications available in WHO database. [4]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases and data mining are sufficient to support a causal association between Etoposide and the risk of Electrolytes imbalance. 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:

1. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012–. Etoposide. 2018 Feb 25. PMID: 31643432. 2022.
2. Shrimanker I, Bhattarai S. Electrolytes. 2022 Jul 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 31082167.
3. Saudi Vigilance (2023). retrieved from: https://ade.sfda.gov.sa [accessed 16/03/2023]
4. Vigilyze.who-umc.org. 2021. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed 7/29/2021].
5. World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at https://www.who.int/publications/m/item/WHO-causalityassessment [Accessed 16/03/2023].