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 Tioguanine and the Risk of Nausea

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

Introduction

Thioguanine is a purine analog of guanine used to treat acute non-lymphocytic leukemia [1]. It belongs to the group of medicines known as antimetabolites [1]. The drug interferes with the growth of cancer cells by blocking the synthesis and metabolism of purine nucleotides [2]. Nausea is an uneasiness of the stomach that often accompanies the urge to vomit, but doesn't always lead to vomiting [3]. The aim of this review is to evaluate the risk of Nausea associated with the use of Tioguanine and 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 Thioguanine and the risk of Nausea [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 103 global Individual case safety reports (ICSRs) as of February 2021 [4]. The reviewers have selected and assessed the causality for top quality reported cases (27 ICSRs). Out of 27 assessed ICSRs, 24 reports provided supportive association with 18 positive dechallenges [5].

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. The results of (IC= -0.2) revealed a negative statistical association for the drug/ADR combination, meaning "Nausea" with the use of "Thioguanine" has been slightly observed less than expected compared to other medications available in WHO database [4].

Literature Upon conducting a literature search, evidences supporting this signal were found.

In a review of randomized controlled trials (RCTs), one of the most frequently observed dose-dependent adverse events of Tioguanine was Nausea in a cohort of 32 patients that led to drug discontinuation in 2 of them [6]. Furthermore, in a clinical study involved 37 patients with chronic active Crohn's disease, 10 patients on 40 mg/day of Thioguanine developed Nausea during a follow up period of 24 weeks [7].

Conclusion

The weighted cumulative evidence identified from the reported cases and literature are sufficient to support a causal association between thioguanine and the risk of nausea. 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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3. Cleveland clinic, Nausea & vomiting Available at: https://my.clevelandclinic.org/health/symptoms/8106-nausea--vomiting
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