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 m ore 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"

29-10-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Cytarabine and the Risk of Palmar plantar erythrodysaesthesia syndrome

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

Introduction

Cytarabine is cytotoxic to a wide variety of proliferating mammalian cells in culture. It exhibits cell phase specificity, primarily killing cells undergoing DNA synthesis (S-phase) and under certain conditions blocking the progression of cells from the G1 phase to the S-phase. Cytarabine Injection in combination with other approved anti-cancer drugs is indicated for remission induction in acute non-lymphocytic leukemia of adults and pediatric patients. It has also been found useful in the treatment of acute non-lymphocytic leukemia and the blast phase of chronic myelocytic leukemia. [1] Palmar-plantar erythrodysesthesia (PPE) or hand-foot syndrome (HFS) is a relatively common side effect of cytotoxic chemotherapy. The initial symptoms are dysesthesia and tingling in the palms, fingers and soles of feet and erythema, which may progress to burning pain with dryness, cracking, desquamation, ulceration and oedema. Palms of the hands are more frequently affected than soles of the feet. [2] The aim of this review is to evaluate the risk of Palmar plantar erythrodysaesthesia syndrome associated with the use of Cytarabine 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 Palmar plantar erythrodysaesthesia syndrome and Cytarabine use. The search conducted on September 2025.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 150 global case-reports while one local case found triggering this investigation. The authors used signal detection tool (Vigilyze) to retrieve global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs with completeness score 1.0-0.9 (30 cases). [4] Among them, nineteen cases were probably and possibly linked to Cytarabine, while the remaining eleven cases assessed as unlikely.

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 (1.8) for this drug/ADR combination which reflects positive statistical association. [4]

Literature: A literature search was conducted by the Signal Team to identify publications related to this ADR in association with Cytarabine. Three publications were identified that reported a link between PPE and the use of Cytarabine. [5-7]

Additional evidence: This ADR is listed in other country drug monograph under skin warnings and precautions. [8]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Cytarabine and Palmar plantar erythrodysaesthesia syndrome. 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:

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