



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”

05-02-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Calcium Folate and the Risk of Shivering

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

Introduction

Calcium Folate (Calcium Leucovorin) is indicated to neutralize the immediate toxic effects of folic acid antagonists, e.g. Methotrexate. It is also indicated to treat megaloblastic anemias due to sprue, nutritional deficiency, pregnancy, infancy, liver disease and malabsorption syndrome. ^[1] Chills (Shivering) are caused by rapid muscle contraction and relaxation. They are the body's way of producing heat when it feels cold. It often predicts the coming of a fever or an increase in the body's core temperature. ^[2] The aim of this review is to evaluate the risk of Shivering associated with the use of Calcium Folate 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 Shivering and Calcium Folate use. The search conducted on December 2024.

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 327 global case-reports while ten local cases found. 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 and 0.9 (30 cases). ^[4] Among them, 24 cases were probably and possibly linked to Calcium Folate, two cases were unable to assess due to lack of important information, while the remaining three cases assessed as unlikely.

Conclusion

The weighted cumulative evidence identified from assessed local and global cases are suggestive for causal association between Calcium Folate and Shivering. 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:

- 1- Electronic medicines compendium (emc). Calcium Folate 15mg Tablets. Available at: <https://www.medicines.org.uk/emc/product/6343/smpe>
- 2- Medlineplus.gov. (n.d.). Chills: MedlinePlus Medical Encyclopedia. [online] Available at: [https://medlineplus.gov/ency/article/003091.htm#:~:text=Chills%20\(shivering\)%20may%20occur%20at.](https://medlineplus.gov/ency/article/003091.htm#:~:text=Chills%20(shivering)%20may%20occur%20at.)
- 3- Vigilyze.who-umc.org. 2024. [online] Available at: <https://vigilyze.who-umc.org/>
- 4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at <https://www.who.int/publications/m/item/WHO-causality-assessment>