



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”

27-08-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Calcium gluconate and the Risk of Phlebitis

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

Introduction

Calcium Gluconate Injection is indicated for pediatric and adult patients for the treatment of acute symptomatic hypocalcemia. The intravenous administration of calcium gluconate increases serum ionized calcium level. Calcium gluconate dissociates into ionized calcium in plasma. ^[1] Phlebitis is inflammation of a vein near the surface of the skin. It's not usually serious and often gets better on its own after 1 or 2 weeks. Phlebitis is also sometimes known as superficial thrombophlebitis or superficial vein thrombosis. ^[2] The aim of this review is to evaluate the risk of Phlebitis associated with the use of Calcium gluconate 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 Phlebitis and Calcium gluconate use. The search conducted on May 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 80 global case-reports while no 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 0.8 and above (27 cases). ^[4] Among them, 22 cases were probably and possibly linked to Calcium gluconate, while the remaining five 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 (3.9) for this drug/ADR combination which reflects strong positive statistical association. ^[4]



Literature: The signal team searched the literature to find related publications linking this ADR to Calcium gluconate. The search showed a published case-report of Phlebitis following the use of Calcium gluconate. ^[5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Calcium gluconate and Phlebitis. 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- Nih.gov. (2023). DailyMed - CALCIUM GLUCONATE- calcium gluconate injection, solution. [online] Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8b77c3d2-992d-4261-8421-9cfd07328fbf>
- 2- National Health Service. (2022, December 20). *Phlebitis (superficial thrombophlebitis)*. NHS. Retrieved August 26, 2025, from <https://www.nhs.uk/conditions/phlebitis/>
- 3- Vigilyze.who-umc.org. 2025. [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>
- 5- Chen, S. C. (2010). Calcium gluconate Upper limb deep vein thrombosis: case report. *Reactions*, 1286, 30.