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"

27-08-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Ertapenem sodium and the Risk of Stevens Johnson syndrome

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

Introduction

Ertapenem sodium is a carbapenem antibiotic. It has in vitroactivity against Gram-positive and Gram-negative aerobic and anaerobic bacteria. The bactericidal activity of ertapenem results from the inhibition of cell wall synthesis and is mediated through ertapenem binding to penicillin binding proteins. [1] Stevens-Johnson syndrome (SJS) is a dermatologic emergency, characterized by the presence of epidermal and mucosal bullous lesions involving less than 10% of the total body surface area. It is a rare disease process with an estimated incidence of 2 to 7 cases per million per year. [2] The aim of this review is to evaluate the risk of SJS associated with the use of Ertapenem sodium 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 Stevens Johnson syndrome and Ertapenem sodium use. The search conducted on June 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 18 case-reports globally in addition to a local Saudi case, which was the trigger for this investigation. The authors used signal detection tool (Vigilyze) to retrieve global cases. [3] Authors also applied WHO-UMC causality assessment criteria on all the extracted local and global ICSRs (19 cases). [4] Among them, two were assessed as probably or possibly linked to Ertapenem sodium, five were considered unlikely, and the remaining twelve could not be assessed due to insufficient information.

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

Literature: The signal team searched the literature to find related publications linking this ADR to Ertapenem sodium. The search showed a published case-report of Stevens Johnson syndrome following the use of Ertapenem sodium. [5]

Additional evidence: Stevens Johnson syndrome is listed in the drug monograph as a warning and precaution for use in other country. [6]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Ertapenem sodium and Stevens Johnson 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:

1- U.S. National Library of Medicine (DailyMed). (2023, December 13). Ertapenem injection.. Retrieved from https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=468105b9-48b3-4477-82c7-e7fb92460e28#S12.4

2- Eyewiki.org. (2018). Stevens-Johnson Syndrome. Available at: https://eyewiki.org/Stevens-Johnson_Syndrome.

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- Ragunathan, K. (2014). Case report: Stevens–Johnson syndrome from ertapenem. Global Journal of Immunology and Allergic Diseases, 2(1), 11–12. https://www.researchgate.net/publication/269602650_Case_Report_Stevens-Johnson_Syndrome_from_Ertapenem

6- Merck Canada Inc. (2023). Ertapenem for injection Product monograph. Government of Canada, Health Canada Drug Product Database. Retrieved from https://pdf.hres.ca/dpd_pm/00072549.PDF