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"

25-09-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Zoster Vaccine 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 (SJS)** associated with the use of **Zoster Vaccine**. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

Introduction

The non-live recombinant adjuvanted herpes zoster vaccine contains small amounts of a surface antigen (protein from the surface) of the virus to stimulate the body to make antibodies against the virus. It also contains an 'adjuvant' which is made of substances to help strengthen the immune responses to the vaccine. The vaccine is used in adults aged 50 years and older to protect against shingles (herpes zoster) and post-herpetic neuralgia (long-lasting nerve pain following shingles). It can also be used from the age of 18 years and over in adults who are at increased risk of herpes zoster. [1] Stevens-Johnson syndrome (SJS) is a rare, serious disorder of the skin and mucous membranes. It's usually a reaction to medication that starts with flu-like symptoms, followed by a painful rash that spreads and blisters. Then the top layer of affected skin dies, sheds and begins to heal after several days. [2] The aim of this review is to evaluate the risk of SJS associated with the use of zoster vaccine 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 SJS and zoster vaccine use. The search conducted on February 2022.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs) of SJS associated with zoster vaccine. While the search resulted in zero reported local cases, the search in the WHO database resulted in 43 global case-reports. The authors used signal detection tool (Vigilyze) to retrieve all reported cases. [3] Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score (0.5) and above (n=16). Among them, 14 cases of Stevens-Johnson syndrome were possibly linked to zoster vaccine.

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, considering the null value equal to zero. The results of (IC= -2.8) revealed a negative statistical association for the drug/ADR combination. [3]

Literature: In February 2022, the author searched for eligible publication using terms "zoster vaccine" and "Stevens-Johnson syndrome".

This signal was detected from a Case series entitled "An Analysis of Spontaneously Reported Data of Vesicular and Bullous Cutaneous Eruptions Occurring Following Vaccination with the Adjuvanted Recombinant Zoster Vaccine." Stevens-Johnson syndrome was one of the identified serious adverse events. [4]

The study objective was to search and analyse 2.5 years of worldwide spontaneously reported post-marketing data for vesicular and bullous cutaneous eruptions that occurred following recombinant zoster vaccine (RZV) vaccination. descriptive analysis was conducted for all identified reports. The analysis of 1928 reports assessed as possible VZV reactivations indicated that the observed number of cases was lower than that expected in the general population. Additionally, 810 reports of non-HZ vesicular and bullous cutaneous eruptions were identified, including injection site rashes attributed to the vaccine's reactogenicity. [4]

Another article was a case report entitled (Stevens-Johnson Syndrome–Like Reaction After Exposure to Pembrolizumab and Recombinant Zoster Vaccine in a Patient with Metastatic Lung Cancer) Was found. An 80-year-old woman with metastatic non–small cell lung cancer who had an SJS-like eruption. The patient presented with a 2-day history of multiple small oral ulcers. She had last taken pembrolizumab 2 days prior and the first dose of RZV 7 days before presentation. An antiseptic solution was prescribed. After 2 days, she developed new ulcers in the tongue. She received treatment with acyclovir without improvement. Subsequently, the patient exhibited worsening of ulcers over the lips and a nonpruritic and nontender rash in the upper back and upper extremities. The patient received prednisone, which slowed the progression of her lesions. She had not been maintained on steroid therapy prior. The patient did not receive the second dose of RZV and pembrolizumab was discontinued. At a 1-month follow-up appointment, her initial eruptions improved. Unfortunately, the patient subsequently presented to the hospital with severe sepsis from a perforated duodenal ulcer. The Author conclude that is possible that the corticosteroids given for her SJS-like syndrome contributed to her death. [5]

Conclusion

The weighted cumulative evidence identified from assessed cases and literature are sufficient to suggest causal association between zoster vaccine 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:

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2- Stevens-Johnson syndrome - Symptoms and causes. (2022). Retrieved 17 February 2022, from https://www.mayoclinic.org/diseases-conditions/stevens-johnson-syndrome/symptoms-causes/syc-20355936
3- Vigilyze.who-umc.org. 2022. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 06/02/2022].
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5- Riano, I., Cristancho, C., & Treadwell, T. (2020). Stevens-Johnson Syndrome–Like Reaction After Exposure to Pembrolizumab and Recombinant Zoster Vaccine in a Patient with Metastatic Lung Cancer. *Journal Of Investigative Medicine High Impact Case Reports*, 8, 232470962091479. doi: 10.1177/2324709620914796