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"

15-02-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Zoster Vaccine and the Risk of Erythema multiforme

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Erythema multiforme** 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] Erythema multiforme is a skin condition considered to be a hypersensitivity reaction to infections or drugs. It consists of a polymorphous eruption of macules, papules, and characteristic "target" lesions that are symmetrically distributed with a propensity for the distal extremities. [2] The aim of this review is to evaluate the risk of Erythema multiforme 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 Erythema multiforme and zoster vaccine use. The search conducted on February 2023.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs) of Erythema multiforme associated with zoster vaccine. While the search resulted in zero reported local cases, the search in the WHO database resulted in 356 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 (0.8) and above (n=22). [4] Among them, 18 cases of Erythema multiforme 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= 0.8) revealed a positive statistical association for the drug/ADR combination. [3]

Literature: On February 2023, the author searched for eligible publication using terms "zoster vaccine" and "Erythema multiforme".

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." Erythema multiforme was one of the identified serious adverse events. [5]

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 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. [5]

In addition, evidences on zoster vaccine and its relation to serious skin reactions were found as well.
In a case report entitled (Bullous fixed drug eruption following administration of the recombinant adjuvant zoster vaccine) was found. A 51-year-old woman with Crohn's disease presented with a bullous rash on her left arm and axilla 2 days after receiving her second dose of the recombinant adjuvant zoster vaccine. She was successfully treated with oral prednisone and topical triamcinolone cream after 1 week of onset. [6]

Another case report entitled (Blistering autoimmune skin reaction following zoster vaccination in an ulcerative colitis patient: Case report and literature review) was found. A 74-year-old woman with history of ulcerative proctosigmoiditis, presented on two occasions with a rash on her face (forehead, cheeks, ears) anterior chest, arms, legs, and abdomen The new rash initially started 40 days after her first zoster vaccine (vaccine was given in April 2019). The rash completely resolved after a 20-day steroid taper with topical corticosteroid for 1–2 weeks and then only as needed for flares. Less than two months after finishing the steroid taper, the patient received the second dose of zoster and had recurrence of the same rash. The patient was treated with oral corticosteroid for one week, and the rash resolved. The second rash occurrence, treatment, and resolution all occurred within less than 2 months of receiving the second vaccination. [7]

Conclusion
The weighted cumulative evidence identified from assessed cases, literature and datamining are sufficient to suggest causal association between zoster vaccine and Erythema multiforme. Health care professionals and health regulators must be aware of the potential risk in vaccine 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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5- Pirrotta, P., Tavares-Da-Silva, F., Co, M., Lecrenier, N., Hervé, C., & Stegmann, J.-U. (2021, October 7). An analysis of spontaneously reported data of vesicular and bullous cutaneous eruptions occurring following vaccination with the adjuvanted recombinant zoster vaccine - drug safety. SpringerLink. Retrieved January 31, 2022, from fhttps://link.springer.com/article/10.1007/s40264-021-01118-3
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