

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”

28-10-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Tirzepatide and the Risk of Depression

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

Introduction

Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. ^[1] Depression is a common but serious mood disorder. It causes severe symptoms that affect how a person feels, thinks, and handles daily activities, such as sleeping, eating, or working. To be diagnosed with depression, the symptoms must be present for at least 2 weeks. There are different types of depression, some of which develop due to specific circumstances. ^[2] The aim of this review is to evaluate the risk of Depression associated with the use of Tirzepatide 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 Depression and Tirzepatide use. The search conducted on July 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 153 global case-reports while five local cases found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. ^[3] Authors also applied WHO-UMC causality assessment criteria on 30 extracted ICSRs with top completeness score of 1.0. ^[4] Among them, 3 cases and possibly linked to Tirzepatide, and 27 cases assessed as not assessable due to lack of valuable 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 (-1.0) for this drug/ADR combination which reflects negative statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Tirzepatide. A study that analysed psychiatric adverse events for Semaglutide, Liraglutide, and Tirzepatide that reported to the EudraVigilance database. It showed that four suicidal reports 3.9% were associated with Tirzepatide. [5]

Conclusion

The weighted cumulative evidence identified from assessed local and global cases and literature are suggestive for causal association between Tirzepatide and Depression. 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- DailyMed - OZEMPIC- Tirzepatide injection, solution (no date) U.S. National Library of Medicine. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=adec4fd2-6858-4c99-91d4-531f5f2a2d79> [Accessed: 25/07/2024].
- 2- Depressive disorder (depression) (no date) World Health Organization. Available at: [https://www.who.int/news-room/fact-sheets/detail/depression#:~:text=Depressive%20disorder%20\(also%20known%20as,and%20feelings%20about%20everyday%20life](https://www.who.int/news-room/fact-sheets/detail/depression#:~:text=Depressive%20disorder%20(also%20known%20as,and%20feelings%20about%20everyday%20life). [Accessed: 25/07/2024].
- 3- Vigilyze.who-umc.org. 2024. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed: 26/07/2024].
- 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> [Accessed: 26/07/2024].
- 5- Tobaiqy, M., & Elkout, H. (2024). Psychiatric adverse events associated with semaglutide, liraglutide and tirzepatide: a pharmacovigilance analysis of individual case safety reports submitted to the EudraVigilance database. International journal of clinical pharmacy, 46(2), 488-495.