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 Semaglutide and the Risk of Optic ischaemic neuropathy

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

Introduction

Semaglutide is a type 2 diabetes medication that acts as a glucagon-like peptide-1 (GLP-1) receptor agonist.It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Also to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. [1] Nonarteritic anterior ischemic optic neuropathy (NAION) is the second most prevalent type of optic neuropathy. It occurs when the short posterior ciliary arteries, responsible for supplying the front part of the optic nerve head, become blocked. This blockage leads to swelling of the nerve fibers (axonal edema) and creates a compartment syndrome within the crowded optic disc causing vision loss. [2] The aim of this review is to evaluate the risk of Optic ischaemic neuropathy associated with the use of Semaglutide 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 Optic ischaemic neuropathy and Semaglutide 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 36 global case-reports for the term (Optic ischaemic neuropathy) and 90 global cases for the term (blindness), while no 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 10 extracted ICSRs with

completeness score of 0.8 and above. [4] Among them, 2 cases were probably and possibly linked to Semaglutide, while the remaining 2 case 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 (3.2) 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 Semaglutide. A retrospective cohort observational study was found. It investigated the association between semaglutide and risk of nonarteritic anterior ischemic optic neuropathy (NAION). The study's findings suggest an association between semaglutide and NAION. The cumulative incidence of NAION for the semaglutide vs non-GLP-1 RA cohorts over 36 months was 6.7% (95% CI, 3.6%-9.7%) and 0.8% (95% CI, 0%-1.8%), respectively. A Cox proportional hazards regression model showed a higher risk of NAION for patients prescribed semaglutide (HR, 7.64; 95% CI, 2.21-26.36; P < .001). [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, literature and disproportionality analysis are suggestive for causal association between Semaglutide and Optic ischaemic neuropathy. 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- semaglutide 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: 10/07/2024].

2- Berry, S. et al. (2017) 'Nonarteritic anterior ischemic optic neuropathy: Cause, effect, and management', Eye and Brain, Volume 9, pp. 23–28. doi:10.2147/eb.s125311. [Accessed: 17/07/2024].

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 21/07/2024].

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: 22/07/2024].

5- Hathaway, J.T. et al. (2024) 'Risk of nonarteritic anterior ischemic optic neuropathy in patients prescribed SEMAGLUTIDE', JAMA Ophthalmology [Preprint]. doi:10.1001/jamaophthalmol.2024.2296.