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"

11-03-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Exenatide and the Risk of Thyroid cancer

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

Introduction

Exenatide is a 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] Thyroid cancer is a disease in which malignant cells form in the tissues of the thyroid gland. The thyroid is a gland at the base of the throat near the trachea. Signs of thyroid cancer include a swelling or lump in the neck. [2] The aim of this review is to evaluate the risk of Thyroid cancer associated with the use of Exenatide 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 Thyroid cancer and Exenatide use. The search conducted on January 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 243 global case-reports. [3] Authors also applied WHO-UMC causality assessment criteria on a sample of 30 cases with completeness score 0.5 and above [4]. Among them, one case were possibly linked to Exenatide, while the remaining 29 cases were lacking of important information for proper assessment.

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 (3.5) 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 Exenatide. The search showed two articles describing the risk of thyroid cancer following the use of GLP-1 receptor agonists. [5,6]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Exenatide and Thyroid cancer. 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- 1- DailyMed - byetta- exenatide injection (no date) U.S. National Library of Medicine. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=53d03c03-ebf7-418d-88a8-533eabd2ee4f

2- Thyroid cancer treatment (no date) Thyroid Cancer Treatment - NCI. Available at: https://www.cancer.gov/types/thyroid/patient/thyroid-treatment-pdq#:~:text=Thyroid%20cancer%20is%20a%20disease,the%20risk%20of%20thyroid%20cancer.

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- Liang, C. et al. (2018) 'Exenatide use and incidence of pancreatic and thyroid cancer: A retrospective cohort study', Diabetes, Obesity and Metabolism, 21(4), pp. 1037–1042. doi:10.1111/dom.13597.

6- Bezin, J. et al. (2022) 'GLP-1 receptor agonists and the risk of thyroid cancer', Diabetes Care, 46(2), pp. 384–390. doi:10.2337/dc22-1148.