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"

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Saudi Food and Drug Authority (SFDA) – Safety Signal of Dulaglutide and the Risk of Dysgeusia

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

Introduction

Dulaglutide works as an agonist of a long-acting glucagon-like peptide 1 (GLP-1) receptor. The molecule consists of 2 identical disulfide-linked chains, each containing a modified human GLP-1 analogue sequence covalently linked to a modified human immunoglobulin G4 (IgG4) heavy chain fragment (Fc) by a small peptide linker. It is indicated to be used for type2 diabetes in adults [1]. Dysgeusia is the persistent of unpleasant, abnormal, or altered taste sensation. It can be described as metallic taste. The disturbance time can be short or long term [2]. The aim of this review is to evaluate the risk of dysgeusia associated with the use of dulaglutide and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between dulaglutide and the Risk of Dysgeusia [3]. We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [4].

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 193 global ICSRs as of January 2021 [3]. The reviewers have selected and assessed the causality for the well-documented ICSRs with completeness scores of 0.6 and above (18 ICSRs); the value 1.0 indicated the highest score for best-written ICSRs. Among the reviewed cases, six of them provides supportive association (1 probable, and 5 possible cases). In Canadian vigilance online database, a spontaneous case-report for this drug/ADR is available. A 58 years old female who experienced dysgeusia after the use of dulaglutide. The patient is taking concomitant medications however, none of them is known to cause this ADR (sitagliptin, citalopram, irbesartan and vitamin-d) [5].

Data Mining: 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= 0.5) revealed a positive statistical association for the drug/ADR combination, which means "Dysgeusia" with the use of "Dulaglutide" have been observed more than expected when compared to other medications available in WHO database [3].

Literature Upon conducting a literature search, several articles found supporting the association:

In a phase IV clinical study that examine dulaglutide and taste impaired (Dysgeusia), the ADR was found to affect 0.53% (174 out of 33,008), especially for people who are female, 60+ old and have been taking the drug for <1 month [6]. Another study showed evidence on class effect of glucagon like peptide-1 (glp-1) analogues (exenatide or liraglutide). Dysgeusia was mentioned as one of the post marketing surveillance ADRs [7].

Conclusion

The weighted cumulative evidences identified from the reported cases, Data mining, and literature are sufficient to support a causal association between dulaglutide and the risk of dysgeusia. Health regulators and health care professionals must be aware of this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

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. Eli Lilly and Company. Saudi Summary of Product Characteristics (SPC) of Dulaglutide (Trulicity) ®; (retrieved from EURS). [Accessed 1/12/2021]
2. Science Direct (2002), Dysgeusia https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/dysgeusia [Accessed 1/21 /2021].
3. Uppsala Monitoring Center (UMC) (2021), Vigilyze database; Available at: https://vigilyze.who-umc.org [Accessed 1/12/2021].
4. Uppsala Monitoring Center (UMC) (2021), The use of the WHO-UMC system for standardized case causality assessment; Available at https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf?ua=1 [Accessed 1/12/2021].
5. Health Canada (2019). Canada Vigilance Adverse Reaction Online Database. Retrived from: https://cvp-pcv.hc-sc.gc.ca/arq-rei/ [Accessed 1/17/2021].
6. Ehealthme (2020), retrieved from: https://www.ehealthme.com/ds/trulicity/taste-impaired/ Accessed 1/21/2021].
7. Shared Care Protocol: Addition of a glucagonlike peptide-1 (GLP-1) analogues (exenatide or liraglutide) to patients already on insulin who have poorly controlled type 2 diabetes. Retrieved from https://hertsvalleysccg.nhs.uk/application/files/7015/3633/4542/GLP-1_analogue_added_to_insulin_201207SCG.pdf [Accessed 1/21/2021].