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"

20-9-2021

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

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Diverticulitis** 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]. Diverticula described as small, bulging pouches that exists in the lining of the digestive system. The presence of diverticula is known as diverticulosis [2]. The aim of this review is to evaluate the risk of Diverticulitis 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 Diverticulitis [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 31 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 (6 ICSRs); the value 1.0 indicated the highest score for best-written ICSRs. Among the reviewed cases, about half of them provides supportive association (1 probable, and 3 possible cases). In addition, the Canadian Vigilance Adverse Reaction Online Database reported a case of 57-year-old male with history of type 2 DM managed by dulaglutide, metformin and insulin glargine, the report mentioned that patient experienced diverticulitis but no clear time to onset was stated [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. The results of (IC= 0.4) revealed a positive statistical association for the drug/ADR combination, which means "Diverticulitis" with the use of "Dulaglutide" have been observed more than expected when compared to other medications available in WHO database [3].

Additional Evidence: The U.S. FDA Centre for Drug Evaluation and Research have published Dulaglutide New Drug Application (NDA) report, which contains data on the safety and efficacy. A case report of a 53 year old male with history of Gastroesophageal Reflux Disease (GERD). The patient experienced erosive diverticulum after 330 days of Dulaglutide use [6].

Conclusion

The weighted cumulative evidences identified from the reported cases and data mining sufficient to support a causal association between Dulaglutide and the risk of Diverticulitis. 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]
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3. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org [Accessed 10/4/2020].
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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. Center for Drug Evaluation and Research (2014) Retrieved from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/125469Orig1s000MedRedt.pdf [Accessed 1/20/2021].