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"

24-11-2021

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

The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of ***Arthralgia*** *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 type II diabetes mellitus in adults [1]. Arthralgia is joints pain (can be one or more of your joints) that can be described as sharp, dull, stabbing, burning or throbbing, and may range in intensity from mild to severe [2]. The aim of this review is to evaluate the risk of Arthralgia 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 Arthralgia [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 190 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 (26 ICSRs); the value 1.0 indicated

the highest score for best-written ICSRs. Among the reviewed cases, about half of them provides supportive association (2 probable, and 8 possible cases).

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= -1.8) revealed a negative statistical association for the drug/ADR combination, which means "Arthralgia" with the use of "Dulaglutide" have been observed less than expected when compared to other medications available in WHO database [3].

Literature: Upon conducting a literature search, there were several evidences supportive for the association:

One randomized controlled trial studied the efficacy and safety of Dulaglutide versus Sitagliptin in type 2 diabetes mellitus patients. As compared to Sitagliptin and placebo, dulaglutide showed higher rate of arthralgia after 26 and 52 weeks of treatment [5]. Another randomized controlled trial studied the efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes (AWARD-1). The results showed an increased number of Arthralgia in patients treated with GLP-1 agonist (Dulaglutide and Exenatide) as compared to placebo [6].

Conclusion

The weighted cumulative evidences identified from the reported cases and literature are sufficient to support a causal association between Dulaglutide and the risk of Arthralgia. 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. Health grades (2021), Arthralgia. https://www.healthgrades.com/right-care/bones-joints-and-muscles/arthralgia [Accessed 1/12/2021].
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. Nauck et al (2014) Efficacy and Safety of Dulaglutide Versus Sitagliptin After 52 Weeks in Type 2 Diabetes in a Randomized Controlled Trial (AWARD-5) retrieved from: https://care.diabetesjournals.org/content/diacare/archive/37/8/2149/1.full.pdf [Accessed 1/18/2021].
6. Wysham et al, (2014)Efficacy and Safety of Dulaglutide Added Onto Pioglitazone and Metformin Versus Exenatide in Type 2 Diabetes in a Randomized Controlled Trial (AWARD-1) https://care.diabetesjournals.org/content/diacare/archive/37/8/2159/1.full.pdf [Accessed 1/18/2021].