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 Sitagliptin and the Risk of Vertigo

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

Introduction

Sitagliptin is dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of patients with type II diabetes mellitus [1]. Inhibition of DPP-4 activity by Sitagliptin enhances fasting and postprandial levels of the intact incretins, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These incretins play a role in glucose homeostasis by increasing insulin release in response to a meal; GLP-1 also decreases glucagon release [2]. Vertigo is a sensation of feeling off balance. Individuals with Vertigo might feel like they are spinning or that the world around them is spinning. Most often, Vertigo is a clinical manifestation of inner ear problem [3]. The aim of this review is to evaluate the risk of Vertigo associated with the use of Sitagliptin 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 Sitagliptin and the Risk of Vertigo [4]. We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [5].

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 89 global Individual case safety reports (ICSRs) as of 2021 [4]. The reviewers have selected and assessed the causality for top quality reported cases (30 ICSRs). Nearly 80% of assessable ICSRs were

supportive for association with 9 probable and 15 possible associations. Moreover, positive dechallenge was reported in 11 cases [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= -0.9) revealed a negatove statistical association for the drug/ADR combination, meaning "Vertigo" with the use of "Sitagliptin" has been observed less slightly than expected compared to other medications available in WHO database [4].

Literature

A randomized controlled trial conducted to investigate safety and efficacy of Sitagliptin as monotherapy in patients with type II diabetes mellitus. The participants (n=103) were randomized to receive Sitagliptin 100 mg once daily or 200 mg once daily compared to placebo. Incidence of Vertigo in Sitagliptin 100 mg study arm was 2%. Vertigo was not reported in patients taking placebo [6]. In addition, Investigators from Colombian Diabetes Association and Diabetes & Glandular Disease Research Associates, Texas examined efficacy and safety of Sitagliptin as monotherapy on glycemic control in patients with type II diabetes mellitus. Participants (n=721) were randomly assigned to receive either Sitagliptin 100 mg or 200 mg daily. Vertigo was reported in 3 (1.3%) of participants receiving 100 mg and 2 (0.8%) in participants receiving 200 mg [7]. Moreover, An analysis of previously published 12 clinical trials to assess safety and tolerability of Sitagliptin in patients with type II diabetes mellitus included data of total 6139 patients. The intervention group was defined as patients treated with Sitagliptin monotherapy or in combination with other antihyperlipidemic agents and the control group was defined as patients taking other antihyperglycemic agents without Sitagliptin. Among 3415 patients
received Sitagliptin at 100 mg once daily, 24 (0.7%) reported Vertigo as adverse event compared to 27 patients (1%) in non-exposed group [8]. However, study findings are relatively accepted since range of other comparator antihyperlipidemic drugs have labelled risk of Vertigo.

Conclusion

The weighted cumulative evidence identified from the reported cases and literature are sufficient to support a causal association between Sitagliptin and the risk of Vertigo. 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:

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