# 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"*

**01-03-2023**

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## Saudi Food and Drug Authority (SFDA) – Safety Signal of Sitagliptin and the Risk of Fatigue

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Fatigue** 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 T2D. [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] Fatigue is a term that refers to a general feeling of exhaustion or a lack of energy. It's not the same as feeling sleepy or drowsy. When you're tired, you don't have any motivation or energy. Sleepiness is a symptom of fatigue, but it is not the same as fatigue. [3] The aim of this review is to evaluate the risk of Fatigue associated with the use of Sitagliptin 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 Fatigue and Sitagliptin use. The search conducted on February 2023.

### Results

**Case Review:** Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The Suadi national database resulted in one reported local case. The WHO database resulted in 629 global case-reports. The authors used signal detection tool (Vigilyze) to retrieve all reported cases. [4] Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score (1.0) and above (n=19). [5] Among them, 7 cases of fatigue were either probably or possibly linked to sitagliptin.

**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, considering the null value equal to zero. The results of (IC= -1.3) revealed a negative statistical association for the drug/ADR combination. [4]

**Literature:** On February 2023, the author searched for eligible publication using terms "Sitagliptin" and "Fatigue".

In a published study reviewed 15 case-reports of patients treated with Sitagliptin. Twelve cases reported Fatigue onset within 1-8 weeks of starting therapy. Furthermore, of the 12 patients, five patients had had fatigue reoccurrence with Sitagliptin re-administration (5 positive re-challenge). [6]

**Class effect:** Saxagliptin and Vildagliptin are dipeptidyl peptidase-4 (DPP-4) inhibitors and has labelled risk of Fatigue. [7-8]

**Conclusion**

The weighted cumulative evidence identified from assessed cases, literature and other medications from the same class are sufficient to suggest causal association between Sitagliptin and Fatigue. 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:**


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