

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”

18-05-2026

Saudi Food and Drug Authority (SFDA) – Safety Signal of Linagliptin and the Risk of Diarrhea

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

Introduction

Linagliptin is used along with diet and exercise and sometimes with other medications to lower blood sugar levels in patients with type 2 diabetes. Linagliptin is in a class of medications called dipeptidyl peptidase-4 (DPP-4) inhibitors. It works by increasing the amounts of certain natural substances that lower blood sugar when it is high. ^[1] Diarrhea — loose, watery and possibly more-frequent passage of stool — is a common condition. Sometimes, it's the only symptom of a condition. Luckily, diarrhea is usually short-lived, lasting no more than a few days. But when diarrhea lasts beyond a few days, it is usually a clue to another problem — such as medicine side effects, changes in diet, irritable bowel syndrome (IBS), or a more serious disorder, including ongoing infection, celiac disease or inflammatory bowel disease (IBD). ^[2] The aim of this review is to evaluate the risk of Diarrhea associated with the use of Linagliptin 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 potential link between Diarrhea and Linagliptin use.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 2390 global case reports while one local cases found that triggers this investigation. The authors used signal detection tool (Vigilyze) to retrieve global cases. ^[3] The author applied Who Causality assessment tool on top 30 cases with completeness score 1.0. ^[3] Among them, 15 cases were probably linked to Linagliptin, 12 cases resulted in possible association, and 3 cases resulted in unlikely association.

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. The IC result is (1.7) for this drug/ADR combination which reflects positive statistical association. ^[3]



Literature: The signal team conducted a literature search to identify publications linking this adverse drug reaction to Linagliptin. The search identified multiple published studies suggesting a possible association between the drug and this potential risk. ^{[4][5][6]}

Conclusion

The weighted cumulative evidence identified from assessed local and global cases alongside with literature and disproportionality analysis are suggestive for causal association between Linagliptin and Diarrhea. 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@sfd.gov.sa

References

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- 2- Mayo Clinic Staff. (2023, August 11). Diarrhea: Symptoms and causes. Mayo Clinic. <https://www.mayoclinic.org/diseases-conditions/diarrhea/symptoms-causes/syc-20352241>
- 3- Vigilyze.who-umc.org. 2026. [online] Available at: <<https://vigilyze.who-umc.org/>>
- 4- National Library of Medicine. (2025). Linagliptin tablet, film coated. DailyMed. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=cdbbd4b2-c07b-00e1-e053-2995a90a5fc9>
- 5- Wu, S., Hopper, I., Skiba, M., Krum, H., & Yang, Y. (2017). Gastrointestinal adverse events of dipeptidyl peptidase-4 inhibitors in type 2 diabetes: A systematic review and network meta-analysis. *Clinical Therapeutics*, 39(9), 1780–1789. <https://doi.org/10.1016/j.clinthera.2017.07.012>
- 6- Bayoumy, A. B., Masclee, G., de Boer, N. K., Neefjes-Borst, A., & Stenvers, D. J. (2025). Inflammatory Bowel Disease in a Patient Returning from Colombia: Association with Dipeptidyl Peptidase 4 Inhibitor?. *Case reports in gastroenterology*, 19(1), 89-95.