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 m ore 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"

08-10-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Lenvatinib and the Risk of Tumour lysis syndrome

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

Introduction

Lenvatinib is indicated for differentiated thyroid cancer, renal cell carcinoma, hepatocellular carcinoma and endometrial carcinoma. Lenvatinib is a kinase inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). [1] Tumour lysis syndrome (TLS) is an oncological emergency characterised by metabolic and electrolyte abnormalities that can occur after the initiation of any cancer treatment, but can also occur spontaneously. It is caused by rapid breakdown of large numbers of cancer cells and subsequent release of large amounts of intracellular content (potassium, phosphate, nucleic acids) into the bloodstream, which overwhelms normal homeostatic mechanisms resulting in hyperuricaemia, hyperphosphataemia, hyperkalaemia, and/or hypocalcaemia. [2] The aim of this review is to evaluate the risk of Tumour lysis syndrome associated with the use of Lenvatinib 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 Tumour lysis syndrome and Lenvatinib use. The search conducted on August 2025.

Results

Cases 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 68 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs with completeness score 0.8 and above (25 cases). [4] Among them, 12 cases were probably related to Lenvatinib, 11 cases could not be assessed due to insufficient information, and the remaining 2 cases were assessed as unlikely.

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 (3.9) for this drug/ADR combination which reflects strong positive statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Lenvatinib. The search showed two published case-reports of Tumour lysis syndrome following the use of Lenvatinib. [5,6]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Lenvatinib and Tumour lysis syndrome. 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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2- Bestpractice.bmj.com. (n.d.). Tumour lysis syndrome - Symptoms, diagnosis and treatment | BMJ Best Practice. [online] Available at: https://bestpractice.bmj.com/topics/en-gb/936.

3- Vigilyze.who-umc.org. 2025. [online] Available at: https://vigilyze.who-umc.org/

4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at https://www.who.int/publications/m/item/WHO-causality-assessment

5- Shimizu, Y., Sunagozaka, H., Yamagata, K. et al. Lenvatinib-induced tumor lysis syndrome in a patient with advanced hepatocellular carcinoma: a case report. Clin J Gastroenterol 14, 645–649 (2021). https://doi.org/10.1007/s12328-020-01306-1

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