

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”

08-10-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Adalimumab and the Risk of Osteonecrosis

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

Introduction

Adalimumab is a fully human, recombinant monoclonal antibody with high affinity and was the third tumor necrosis factor-alpha (TNF- α) inhibitor. Adalimumab is used to treat various autoimmune conditions such as rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, Crohn disease, and ulcerative colitis. ^[1] Osteonecrosis is a painful condition that involves the death of bone cells due to decreased blood flow. It is also called avascular necrosis (AVN) or aseptic necrosis. It is a painful condition most commonly occurring in the hips or knees and is often more symptomatic with any weight-bearing activities, such as walking. ^[2] The aim of this review is to evaluate the risk of Osteonecrosis associated with the use of Adalimumab 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 Osteonecrosis and Adalimumab use. The search conducted on September 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 351 global case-reports while only one local case found, which triggers this investigation. The authors used signal detection tool (Vigilyze) to retrieve global cases. ^[3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSR with completeness score 0.8 and above (25 cases). ^[4] Among them, eighteen cases were probably and possibly linked to Adalimumab, four unlikely cases, while the remaining three cases could not be assessed due to insufficient information.

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

Conclusion

The weighted cumulative evidence identified from assessed cases and literature are suggestive for causal association between Adalimumab and Osteonecrosis. 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:

- 1- Ellis, C. R., & Azmat, C. E. (2020). Adalimumab.
- 2- Osteonecrosis (no date) rheumatology.org. Available at: <https://rheumatology.org/patients/osteonecrosis>.
- 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- Sisalli et al. (2023) – “Medication-Related Osteonecrosis of the Jaw: A Case Report of an Unusual Side Effect of Adalimumab”
- 6- Cassoni et al. (2016) – “Adalimumab: Another Medication Related to Osteonecrosis of the Jaws?”