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"

10-09-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Denosumab and the Risk of Autoimmune Hepatitis

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

Introduction

Denosumab is a human monoclonal IgG2 antibody that attaches to RANKL (receptor activator of NFκB ligand) with high specificity and affinity, preventing interaction with RANK on the osteoclast membrane. This binding inhibits osteoclast differentiation, activation, and survival, ultimately promoting bone formation and reducing the risk of fractures. [1] Autoimmune Hepatitis (AIH) is an immune-mediated inflammatory liver disease of uncertain cause which affects all ages, both genders, and all ethnicities. Patients may be asymptomatic, chronically ill, or present with acute liver failure (ALF). [2] The aim of this review is to evaluate the risk of Autoimmune Hepatitis associated with the use of Denosumab 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 Autoimmune Hepatitis and Denosumab use. The search conducted on July 2024.

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 13 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs. [4] Among them, 5 cases were possibly linked to Denosumab, and 7 cases assessed as not assessable due to lack of valuable information, while the remaining 1 case assessed as unlikely.

Literature:
The author searched for eligible publications using the terms "Denosumab "and "of "Autoimmune Hepatitis". As a result, three published case-reports found supportive for this signal. [5-7]

Conclusion
The weighted cumulative evidence identified from assessed cases and literature are suggestive for causal association between Denosumab and Autoimmune Hepatitis. 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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