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"

7-3-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Natalizumab and the Risk of Acute Coronary Syndrome

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

Introduction Natalizumab is a selective adhesion-molecule inhibitor and binds to the α4-subunit of human integrins, which is highly expressed on the surface of all leukocytes, with the exception of neutrophils. Natalizumab is approved in Saudi Arabia as a single disease modifying therapy in highly active relapsing remitting multiple sclerosis [1]. Acute coronary syndrome (ACS) represents the continuum of disease representing decreased coronary blood flow and acute myocardial ischemia and/or infarction [2]. The aim of this review is to evaluate the risk of acute coronary syndrome associated with the use of natalizumab and to suggest regulatory recommendations if required.

Methodology Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between natalizumab and the risk of acute coronary syndrome [3]. We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [4].

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 542 global ICSRs as of July 19th 2020 [3]. The reviewers have selected and assessed the causality for the well-documented ICSRs with completeness scores of 0.9 and above (30 ICSRs); the value 1.0 indicated the highest score for best-written ICSRs. Among the reviewed cases, more than half of them provides supportive association (6 probable and 8 possible cases) and 10 positive dechallenges.

Data Mining: 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= -1.4) revealed a negative statistical association for the drug/ADR combination, which means "Acute Coronary Syndrome" with the use of "Natalizumab " have been observed less than expected when compared to other medications available in WHO database [3].

Supportive Evidences: Some cardiac disorders associated with natalizumab may potentiate the risk of ACS. The risk of tachycardia and angina pectoris have been experienced during the clinical trials of natalizumab as described in approved Canadian drug monograph [5].

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases and other evidences are sufficient to support a causal association between natalizumab and the risk of acute coronary syndrome. Health regulators and health care professionals must be aware for this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

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. TYSABRI (2017), Saudi Summary of Product Characteristics (SPC) Natalizumab; (retrieved from EURS).
2. The Clerkship Directors in Emergency Medicine (CDEM; 2020); Acute Coronary Syndrome (ACS); Available at: https://www.saem.org/cdem/education/online-education/m4-curriculum/group-m4-cardiovascular/acute-coronary-syndromes [Accessed 7/21/2020].
3. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org/ [Accessed 9/21/2020]
4. Uppsala Monitoring Center (UMC) (2020), The use of the WHO-UMC system for standardized case causality assessment; Available at https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf?ua=1 [Accessed 23/7/2020].
5. Canadian Health (CA). Natalizumab Product Monograph (2017); available at: https://pdf.hres.ca/dpd_pm/00039755.PDF [accessed 7/21/2020].