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"

7-31-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Docetaxel and Risk of Rhabdomyolysis

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

Introduction

Docetaxel is a second-generation chemotherapeutic agent of the taxane family. A derivative of paclitaxel, the first taxane to hit the market, docetaxel's primary mechanism of action is to bind beta-tubulin, enhancing its proliferation and stabilizing its conformation. It is indicated for breast cancer, non-small cell lung cancer, prostate cancer, head and neck cancer and gastric adenocarcinoma. [1] Rhabdomyolysis is a complex medical condition involving the rapid dissolution of damaged or injured skeletal muscle. This disruption of skeletal muscle integrity leads to the direct release of intracellular muscle components, including myoglobin, creatine kinase (CK), aldolase, and lactate dehydrogenase, as well as electrolytes, into the bloodstream and extracellular space. [2]

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 Docetaxel and the risk of rhabdomyolysis. [3] WHO-Uppsala Monitoring Centre (UMC) criteria have been used 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 is 41 global Individualized Case Safety Reports (ICSRs) as of March 2022. [3] The causality assessment resulted in four probable case, eight possible cases and three unlikely cases. Twenty-six cases were unassessable.
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 result of (IC= -1.9)

revealed a negative statistical association for the drug/ADR combination, which means "rhabdomyolysis" with the use of "Docetaxel" have been observed less than expected when compared to other medications available in WHO database. [3]

Literature Review: A case report entitled (A Case of Docetaxel-Induced Rhabdomyolysis) was found. A female patient who ware recently diagnosed lobular carcinoma of the left breast for which she had a left mastectomy with axillary dissection and prophylactic right mastectomy and received Docetaxel as treatment for that. She developed rhabdomyolysis. [5]

Regulatory agencies: The signal was detected from FDA Adverse Event Reporting System (FAERS). FDA is still evaluating the need for regulatory action. [6]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Docetaxel and the risk of rhabdomyolysis. Health regulators and health care professionals must be aware of 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. Aventis Pharma S.A.. Saudi Summary of Product Characteristics (SPC) of Docetaxel (TAXOTERE).2016 (retrieved from: EURS). [Accessed 3/7/2022]
2. Du Q, Jiang G, Li S, Liu Y, Huang Z. Docetaxel increases the risk of severe infections in the treatment of non-small cell lung cancer: a meta-analysis. Oncoscience. 2018;5(7-8). doi:10.18632/oncoscience.444]
3. Vigilyze.who-umc.org. 2021. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed 53/7/2022].
4. Uppsala Monitoring Center (UMC) (2022), 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 3/7/2022]
5. Thalambedu N, Atiq MU, Patel S. A Case of Docetaxel-Induced Rhabdomyolysis. Cureus. Published online 2020. doi:10.7759/cureus.9380
6. U.S. Food and Drug Administration. 2022. April - June 2021 | Potential Signals of Serious Risks/New Safety Info. [online] Available at: <https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/april-june-2021-potential-signals-serious-risksnew-safety-information-identified-fda-adverse-event> [Accessed 3/6/2022].