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"

2-3-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Imatinib and the Risk of Polyserositis

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

Introduction Imatinib mesylate is a protein-tyrosine kinase inhibitor that inhibits the bcr-abl tyrosine kinase which is the abnormal tyrosine kinase that created by the Philadelphia chromosome abnormality in chronic myeloid leukemia (CML) [1]. Imatinib is indicated for the treatment of adult patients with newly diagnosed, Philadelphia chromosome-positive, chronic myeloid leukemia (CML) in chronic phase [2]. Polyserositis is defined as general inflammation of serous membranes that has associated with serous effusion [3]. The aim of this review is to evaluate the risk of Polyserositis associated with the use of Imatinib 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 Imatinib and the Risk of Polyserositis [4] We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [5]

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 11 global ICSRs as of November 15, 2020 [4]. The reviewers have selected all cases (11 ICSRs); among the reviewed cases, about half of them provides supportive association (4 possible association cases and 2 positive dechallenge).

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= 3)

revealed a positive statistical association for the drug/ADR combination, which means " Polyserositis" with the use of "Imatinib " have been observed noticeably more than expected when compared to other medications available in WHO database [4].

Supportive Evidences: According to a report published by WHO in 2011 on polyserositis, 5 out of 151 cases of polyserositis were associated with imatinib on VigiBase database. Four out of these five cases, were patients whom used imatinib alone however all of them formed polyserositis. The time of onset was three weeks to five years. The reports concludes that, it is appearing that there is an association between imatinib and polyserositis [4].

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, data mining, and WHO report are sufficient to support a causal association between Imatinib and the risk of Polyserositis. Health regulators and health care professionals must be aware for this potential risk of and it is advisable to monitor any signs or symptoms in treated patients is essential.

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. NOVARTIS, https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/021588s009lbl.pdf [Accessed 11/16/2020]
2. Saudi Summary of Product Characteristics (SPC) of imatinib mesylate (KETOVA) ®; (retrieved from EURS).
3. Indian Journal of allergy and asthma and immunology. (2016). Polyserositis DOI: 10.4103/0972-6691.195267. Retrieved from: https://www.ijaai.in/article.asp?issn=0972-6691;year=2016;volume=30;issue=2;spage=102;epage=104;aulast=Das [Accessed 11/16/2020]
4. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org/ [Accessed 9/21/2020]
5. 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].