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"

23-10-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Isotretinoin and the Risk of Blood Growth Hormone Decrease (BGHD)

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

Introduction

Isotretinoin is a form of vitamin A used to treat acne. It is the only therapy that impacts on all of the major etiological factors implicated in acne. The drug has a significant reduction in sebum production, influences comedogenics, lowers surface and ductal P. acnes and has anti-inflammatory properties [1]. Growth hormone is produced by pituitary gland and governs our height, bone length and muscle growth. Adults with growth hormone deficiency (which may result from problems with the pituitary gland or hypothalamus) may have symptoms including: poor bone density and osteoporosis, reduced muscle mass, fatigue, depression, and poor memory [2]. The aim of this review is to evaluate the risk of BGHD associated with the use of Isotretinoin 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 Isotretinoin and the risk of BGHD [3]. We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [4].

Results

Case Review: There were five individual case safety reports (ICSRs) for the combined drug/adverse drug reaction as of March 2022 [3]. Using the WHO causality assessment tool, one case revealed a possible BGHD association with Isotretinoin while the other four were lacking of sufficient data for assessing the causal relationship [4].

Data Mining: Information component (IC), a tool developed by WHO-UMC to measure the reporting ratio, is used to estimate the disproportionality of the observed and expected reporting rates for drug/adverse drug reaction pairs. Positive IC values indicate a statistical association, whereas negative values indicate a weaker statistical association. The results of (IC= 2.7) revealed that the drug/ADR combination has a positive statistical association. In other words, BGHD has been observed more than expected with Isotretinoin compared to other medications in the database [3].

Literature: Investigators assessed effects of different doses of Isotretinoin on pituitary hormones in 105 patients with acne. patients were divided into three groups; the first group received 0.5-1 mg/kg/day, the second 0.2-0.5 mg/kg/day and the third intermittent 0.5-1 mg/kg/day (only 1 week in 1 month) Isotretinoin treatment. Blood samples were collected for biochemistry and hormone analysis, before the treatment and after 3 months. Laboratory screening of patients revealed significant decrease in growth hormone levels ($p = 0.002$) [5].

Conclusion

The weighted cumulative evidence identified from the reported cases, data mining and literature are sufficient to support a causal association between Isotretinoin and the risk of BGHD. 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. Hoffmann-La Roche Ltd (2021). Saudi Summary of Product Characteristics (SPC) of Roaccutane-Isotretinoin Available at: sdi.sfda.gov.sa
2. Bergan-Roller, H. E., & Sheridan, M. A. (2018). The growth hormone signaling system: Insights into coordinating the anabolic and catabolic actions of growth hormone. General and comparative endocrinology, 258, 119–133. https://doi.org/10.1016/j.ygcen.2017.07.028
3. Vigilyze.who-umc.org. 2022. [online] Available at: <https://vigilyze.who-umc.org/>
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
5. Karadag, A. S., Takci, Z., Ertugrul, D. T., Bilgili, S. G., Balahoroglu, R., & Takir, M. (2015). The effect of different doses of isotretinoin on pituitary hormones. Dermatology (Basel, Switzerland), 230(4), 354–359. https://doi.org/10.1159/000375370