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"

20-9-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Clomifene and the Risk of Blindness

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

Introduction

Clomifene (clomiphene) citrate is an orally administered nonsteroidal agent, which has both estrogenic and anti-estrogenic properties used for induction of ovulation since 1962. It is the treatment of choice in women with ovulatory disorders who are normally oestrogenised [1]. Blindness is a lack of vision. It may also refer to a loss of vision that cannot be corrected with glasses or contact lenses [2]. The aim of this review is to evaluate the risk of blindness associated with the use of clomifene 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 clomifene and the risk of Blindness [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 10 global ICSRs as of December 2020 [3]. The reviewers have selected all ICSRs (10 ICSRs). After reviewing the cases, about half of them provides supportive association (1 probable, and 3 possible cases).

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. The results of (IC= 1.4) revealed a positive statistical association for the drug/ADR combination, which means "Blindness " with the use of "Clomifene" have been observed more than expected when compared to other medications available in WHO database [3].

Supportive Evidences: The WHO have published a report which was initiated by the Eritrean Pharmacovigilance Center after receiving one case of retinal detachment that caused irreversible blindness while on use of clomifene citrate. The center did comprehensive assessment for all reported cases in WHO database at that time (2016). They concluded that, case assessment supports a causal association between clomifene citrate and blindness. A case of irreversible blindness due to intake of Clomifene citrate highlights the fact that, ladies undertaking clomifene citrate should be monitored carefully [3].

Clomifene citrate has been associated with several visual problems as stated in local and international drug labels, which may potentiate the risk of blindness. Canadian drug monograph, U.S. FDA drug label, and Saudi Summary of Product characteristics (SPC) have mentioned several visual disorders including but not limited to (blurred vision, cataract, eye pain, macular edema, photophobia, diplopia, scotomata, retinal thrombosis, temporary or prolonged loss of vision, possibly irreversible)[5,6,7].

Conclusion

The weighted cumulative evidences identified from the reported cases, data mining and other supportive evidence are sufficient to support a causal association between clomifene and the risk of blindness. 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:

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