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"

17-05-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Dutasteride and the Risk of Diabetes Mellitus

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

Introduction

Dutasteride is a 5α-reductase inhibitor, indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate [1]. It competitively inhibits type-I & II 5-alpha reductase, resulting in inhibition of the conversion of testosterone to dihydrotestosterone and markedly suppresses serum dihydrotestosterone levels [2]. Diabetes Mellitus (DM) is an array of dysfunctions characterized by hyperglycemia and resulting from the combination of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion [3]. The aim of this review is to evaluate the risk of Diabetes Mellitus associated with the use of Dutasteride and 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 Dutasteride and the risk of Diabetes Mellitus [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 12 global Individual case safety reports (ICSRs) as of November 2021 [4]. The author selected 4 ICSRs that represents completeness score 0.5 and above. Following the causality assessment, 2 ICSRs were supportive for the association. One report revealed probable association with positive dechallenge and the other report revealed possible association [5].

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= -0.6) revealed a negative statistical association [4].

Literature: In a cohort of 230 men aged between 47 and 68 years suffering Benign prostatic hyperplasia (BPH) and treated with Dutasteride. Participants were followed up for 36 to 42 months. Dutasteride resulted in increased blood glucose, glycosylated hemoglobin A, total cholesterol, and low-density lipoprotein cholesterol levels [6]. Furthermore, in a population-based large cohort study enrolled 30000 participants aged 40 and above and prescribed Finasteride, Dutasteride or Tamsulosin for BPH. Dutasteride significantly increased risk of new onset diabetes [Adj. HR 1.34, 95% CI (1.07 to 1.40)] [7].

Conclusion

The weighted cumulative evidence identified from the reported cases and literature are sufficient to support a causal association between Dutasteride and the risk of Diabetes Mellitus. 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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7. Wei L, Lai EC, Kao-Yang YH, Walker BR, MacDonald TM, Andrew R. Incidence of type 2 diabetes mellitus in men receiving steroid 5α-reductase inhibitors: population based cohort study. BMJ. 2019 Apr 10;365:l1204. doi: 10.1136/bmj.l1204. PMID: 30971393; PMCID: PMC6456811.