

## 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”

25-07-2023

### Saudi Food and Drug Authority (SFDA) – Safety Signal of Progesterone and the Risk of Meningioma

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

#### Introduction

Progesterone capsules are an oral dosage form of progesterone, which is chemically identical to progesterone of ovarian origin. It is indicated for use in the prevention of endometrial hyperplasia in nonhysterectomized postmenopausal women who are receiving conjugated estrogens tablets. They are also indicated for use in secondary amenorrhea. <sup>[1]</sup> Meningiomas are the most common benign intracranial tumor. They originate from arachnoid cap cells, which are cells within the thin, spider web-like membrane that covers the brain and spinal cord. Although the majority of meningiomas are benign, these tumors can grow slowly until they are very large, if left undiscovered, and, in some locations, can be severely disabling and life-threatening. <sup>[2]</sup> The aim of this review is to evaluate the risk of Meningioma associated with the use of progesterone and to suggest regulatory recommendations if required.

#### Methodology

Signal Detection team at SFDA performed a signal review using National Pharmacovigilance Center (NPC) database, and World Health Organization (WHO) database, VigiBase, with literature screening to retrieve all related information to assess the causality between Meningioma and Progesterone use. The search conducted on June 2023.

#### Results

**Case Review:** Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 67 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. <sup>[3]</sup> Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score 0.8 and above (n=31). <sup>[4]</sup> Among them, 26 cases of meningioma were possibly linked to progesterone.

**Datamining:** 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 IC result is (5.1) for this drug/ADR combination which reflects high statistical association. <sup>[4]</sup>

### **Conclusion**

The weighted cumulative evidence identified from assessed cases and disproportionality analysis are sufficient to suggest causal association between progesterone and meningioma. Health care professionals and health regulators must be aware of the potential risk in drug recipients.

### **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](mailto:NPC.Drug@sfda.gov.sa)

### **References:**

- 1- DailyMed - progesterone capsule (no date) U.S. National Library of Medicine. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4de0715d-a3b9-42fa-b4e4-6371151fd75c> [Accessed 20/06/2023].
- 2- Meningiomas AANS. Available at: <https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Meningiomas> [Accessed 20/06/2023].
- 3- Vigilyze.who-umc.org. 2023. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed 20/06/2023].
- 4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at <https://www.who.int/publications/m/item/WHO-causality-assessment> [Accessed 20/06/2023].