

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”

7-31-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Ciclosporin and Risk of Respiratory Failure

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

Introduction

Ciclosporin is a cyclic polypeptide consisting of 11 amino acids. It is a potent immunosuppressive agent, which in animals prolongs survival of allogeneic transplants of skin, heart, kidney, pancreas, bone marrow, small intestine or lung. ^[1] Respiratory failure is a clinical condition that happens when the respiratory system fails to maintain its main function, which is gas exchange, in which PaO₂ is lower than 60 mmHg and/or PaCO₂ is higher than 50 mmHg. ^[2]

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 Ciclosporin and the risk of respiratory failure. ^[3] WHO-Uppsala Monitoring Centre (UMC) criteria have been used as standard for assessing the causality of the reported cases. ^[4]

Results

Case Review: The search in the national database resulted in one case and it was unassessable. The number of resulted cases for the combined drug/adverse drug reaction is 348 global Individualized Case Safety Reports (ICSRs) as of May 2022. Cases with completeness score >0.8 were extracted and assessed (n= 26). ^[3] The causality assessment resulted in two probable case, sixteen possible cases and three unlikely cases. Five cases were unassessable.

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 result of (IC= 2) revealed a positive statistical association for the drug/ADR combination, which means “respiratory

failure” with the use of “Ciclosporin” have been observed more than expected when compared to other medications available in WHO database. [3]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Ciclosporin and the risk of respiratory failure. 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. Novartis Pharma AG. (2014).Saudi Summary of Product Characteristics (SPC) of Ciclosporin (Neoral) ® (retrieved from: EURS). [Accessed 5/17/2022]
2. Patel S, Sharma S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jun 24, 2021. Respiratory failure. [PubMed] [Accessed 5/17/2022].
3. Vigilyze.who-umc.org. 2021. [online] Available at: <<https://vigilyze.who-umc.org/>> [Accessed 5/17/2022].
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_effficacy/WHOcausality_assessment.pdf?ua=1> [Accessed 5/17/2022]