

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”

05-02-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Ethambutol and the Risk of Optic atrophy

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

Introduction

Ethambutol is used for the treatment of pulmonary tuberculosis. The medication should not be used as a single regimen but rather in tandem with at least 1 antitubercular drug, such as isoniazid. Ethambutol is effective against Mycobacterium tuberculosis strains but less effective against viruses, fungi, or other bacteria. ^[1] Optic atrophy is the hallmark of damage to the visual pathway. It appears as a pale disc on fundus examination. This clinical appearance is not a disease, it only indicates damage to the anterior visual pathway, which can occur in several conditions. ^[2] The aim of this review is to evaluate the risk of Optic atrophy associated with the use of Ethambutol 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 Optic atrophy and Ethambutol use. The search conducted on December 2024.

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 64 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve global cases. ^[3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSR with completeness score 0.8 and above (24 cases). ^[4] Among them, 14 cases were probably and possibly linked to Ethambutol, two cases were unable to assess due to lack of valuable information, while the remaining eight cases assessed as unlikely.

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 (4.9) for this drug/ADR combination which reflects strong positive statistical association. ^[4]



Conclusion

The weighted cumulative evidence identified from assessed cases and disproportionality analysis are suggestive for causal association between Ethambutol and Optic atrophy. 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

References:

- 1- Lee N, Patel P, Nguyen H. Ethambutol. [Updated 2024 May 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK559050/>
- 2- Ahmad SS, Blair K, Kanukollu VM. Optic Atrophy. [Updated 2024 Mar 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK559130/>
- 3- Vigilyze.who-umc.org. 2024. [online] Available at: <https://vigilyze.who-umc.org/> .
- 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> .