SAFETY COMMUNICATION

21-5-2018

Risk of Death and Serious Adverse Reactions Associated with the Combined Use of Benzodiazepines and Opioids

The Saudi Food and Drug Authority (SFDA) would like to inform Healthcare Professionals (HCPs) about the risk of respiratory depression and death following the combined use of benzodiazepines and opioids.

Opioids are a well-known class of medicines prescribed for pain relief, and they account for approximately one-fourth of prescribed painkillers. Opioids have various opioid receptor subtypes and each has specific function. On the other hand, benzodiazepines are a class of medicines that known to reduce anxiety (anxiolytic), panic attacks, and seizures. They work by enhancing the effect of the neurotransmitter gamma-aminobutyric acid (GABA).

The SFDA initiated the investigation based on a potential signal originating from foreign regulatory authority. The SFDA reviewed all available evidence related to this safety concern including locally and globally reported adverse drug event (ADE) reports that were retrieved form the National Pharmacovigilance Center (NPC) database and World Health Organization (WHO) database (VigiBase). Although there were no locally reported cases, the WHO database revealed 3,840 internationally reported cases for respiratory failure and 1,938 death cases. Both ADEs reported following the combined administration of opioid – benzodiazepine.

In addition, a literature review was conducted to determine the possible association of this signal to the combined medications. As a result, SFDA found multiple supportive studies including (one retrospective cohort study, one prospective cohort study, and one case-cohort study). [1-3]

The SFDA investigations concluded that the current available evidence suggests a probable association between the combined use of benzodiazepine – opioid and the risk of serious adverse drug reactions including respiratory depression and death. Therefore, SFDA requested all benzodiazepine and opioids marketing authorization holders to update the summary of product characteristics (SPC) and patient information leaflet (PIL) to reflect the newly identified risks. These updates include the new boxed warnings, special warnings and precautions for use and drug interactions.

The SFDA will continue its thorough investigations for close monitoring such a drug-event combination and will update all concerned healthcare providers upon availability of new safety data.

Report Adverse Drug Events (ADEs) to the SFDA

The SFDA urges healthcare professionals to report ADEs resulted from combined use of benzodiazepine and opioids to the SFDA using the following contact information:
National Pharmacovigilance and Drug Safety Center (NPC)
Saudi Food and Drug Authority-Drug sector
3292 Northern Ring Road
Al Nafal District
Riyadh 13312 – 6288
Kingdom of Saudi Arabia
Reporting hotline: 19999
Fax: 01 2057662
Email: npc.drug@sfda.gov.sa
Webpage: http://ade.sfda.gov.sa

References:

1. Jones, C. M., & McAninch, J. K. (2015). "Emergency department visits and overdose deaths from combined use of opioids and benzodiazepines." *American Journal of Preventive Medicine, 49*(4), 493–501.

2. Park, T. W., et al. (2015). "Benzodiazepine prescribing patterns and deaths from drug overdose among U.S. veterans receiving opioid analgesics: Case-cohort study." *BMJ, 350,* h2698.

3. Dasgupta, N., et al. (2016). "Cohort study of the impact of high-dose opioid analgesics on overdose mortality." Pain Medicine, 17(1), 85–98.