SAFETY ALERT

DRAP SAFTEY ALERT NO. 34

# Safety Alert of Risk of complex sleep behaviours with Zolpidem

**Date: 11th of April, 2023.**

## Target Audience:

- Manufacturers and importers of Zolpidem;
- Healthcare Professionals; and
- Patients, consumers or caregivers.

## Background:

The Ministry of Health Labour and Welfare (MHLW) and the Pharmaceutical and Medical Device Agency (PMDA) of Japan in July, 2022 have announced that the product information for triazolam, zolpidem, zopiclone and eszopiclone should be revised to include the risk of abnormal behaviour as parasomnia. In addition, the use of triazolam, zolpidem or zopiclone is to be contraindicated in patients who have experienced abnormal behaviour such as parasomnia. Based on the published literature on the pharmacological mechanisms of parasomnia and cases of parasomnia reported in Japan, it was concluded the four drugs can increase the risk of abnormal behaviour as parasomnia, which may lead to serious self/other injuries or accidents. Also, a contraindication is considered necessary for triazolam, zolpidem and zopiclone in patients with a history of drug-induced parasomnia due to the risk of recurrence. Regarding eszopiclone, careful administration is still required but it is not a contraindication at this time, as there have been no reports of parasomnia in Japan for this drug.

Previously, the United States Food and Drug Administration (US-FDA) in April 2019 announced that rare but serious injuries have occurred with some medicines used to treat insomnia such as eszopiclone (Lunesta®), zaleplon (Sonata®) and zolpidem (Ambien®.). The

injuries are a result of sleep behaviours which include: sleepwalking, sleep driving and engaging in other activities while not fully awake. These complex sleep behaviours have also resulted in deaths. Serious injuries and death from complex sleep behaviours have occurred in patients with and without a history of such behaviours, even at the lowest recommended doses, and the behaviours can occur after just one dose. These behaviours can occur after taking these medicines with or without alcohol or other central nervous system depressants that may be sedating such as tranquillizers, opioids, and anti-anxiety medicines. As a result, FDA required information about this risk to be added to the *Boxed Warning*, the FDA's prominent warning and also to the *contraindication* (strongest warning) to avoid use in patients who have previously experienced an episode of complex sleep behaviour with eszopiclone, zaleplon, and zolpidem.

## Action in Pakistan:

Accordingly, the case of the risk of complex sleep behaviours with Zolpidem was discussed in the 2nd meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP), which decided as per Rule 10 (1) (h) (ii), (iv) and (vi) of Pharmacovigilance Rules, 2022 that registration holders should update the prescribing information/safety specification of zolpidem-containing drugs by including information related to complex sleep behaviour in the warning and precaution sections, information related to contraindications in patients who have experienced complex sleep behaviours after taking these drugs in the past, and to create a boxed warning as per the FDA format.

## Therapeutic Goods Affected.

Name: **Zolpidem.** Zolpidem tartrate is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation.

## Advice for patients.

Patients should stop taking Zolpidem and contact their healthcare professionals right away

if they experience a complex sleep behaviour where a patient is engaged in activities while he/she is not fully awake or if the patient do not remember activities they have done while taking the medicine.

## Advice for healthcare professionals.

Healthcare professionals are requested to ask patients and their families or other caregivers at the time of prescribing or dispensing of zolpidem tartrate as to whether the patients have experienced abnormal behaviour as a symptom of parasomnia after they used these drugs in the past. Examples of abnormal behaviour as a symptom of parasomnia include: walking around indoors or outdoors; driving a car; making or eating a meal; making a phone call; behaving violently or calling out, etc. Most of the abnormal behaviours occur after the use of the drug without being fully awake, and those behaviours are not remembered the next day. Healthcare professionals are also advised to not prescribe zolpidem to patients who have previously experienced complex sleep behaviours after taking this medicine. Also, healthcare professionals should advise all patients that although rare, those behaviours have led to serious injuries or death and that if patients experience an episode of complex sleep behaviour, they should discontinue taking the medicines.

## Guidelines for reporting Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with zolpidem medicines to the National Pharmacovigilance Centre, Drug Regulatory Authority of Pakistan through the Med Vigilance E-Reporting System available on the DRAP website. Similarly, ADRs can also be reported through Med Safety App which is available for download from the App Store (for iOS devices) and Google Play (for Android devices).

## References:


1. Minutes of 2nd meeting of Pharmacovigilance Risk Assessment Expert Committee.