衞生署藥物辦公室
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DEPARTMENT OF HEALTH
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DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

FDA adds Boxed Warning for risk of serious injuries caused by sleepwalking with certain prescription insomnia medicines

Your attention is drawn to the US Food and Drug Administration's (FDA) announcement that FDA is advising that rare but serious injuries have happened with certain common prescription insomnia medicines because of sleep behaviors, including sleepwalking, sleep driving, and engaging in other activities while not fully awake. These complex sleep behaviors have also resulted in deaths. These behaviors appear to be more common with eszopiclone (Lunesta), zaleplon (Sonata), and zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist) than other prescription medicines used for sleep.

As a result, FDA is requiring a Boxed Warning, its most prominent warning, to be added to the prescribing information and the patient medication guides for these medicines. FDA is also requiring a Contraindication, its strongest warning, to avoid use in patients who have previously experienced an episode of complex sleep behavior with eszopiclone, zaleplon, and zolpidem.

Serious injuries and death from complex sleep behaviors have occurred in patients with and without a history of such behaviors, even at the lowest recommended doses, and the behaviors can occur after just one dose. These behaviors can occur after taking these medicines with or without alcohol or other central nervous system depressants that may be sedating such as tranquilizers, opioids, and anti-anxiety medicines.

Health care professionals should not prescribe eszopiclone, zaleplon, or zolpidem to patients who have previously experienced complex sleep behaviors after taking any of these medicines. Advise all patients that although rare, the behaviors caused by these medicines have led to serious injuries or death. Tell the patient to discontinue taking these medicines if they experience an episode of complex sleep behavior.

Patients should stop taking their insomnia medicine and contact their health care professional right away if they experience a complex sleep behavior where they engage in activities while they are not fully awake or if they do not remember activities they have done while taking the medicine.

FDA identified 66 cases of complex sleep behaviors occurring with these medicines over the past 26 years that resulted in serious injuries, including death. This number includes only reports submitted to FDA or those found in the medical literature, so there may be additional cases about which FDA is unaware. These cases included accidental overdoses, falls, burns, near drowning, exposure to extreme cold temperatures leading to loss of limb, carbon monoxide poisoning, drowning, hypothermia, motor vehicle collisions with the patient driving, and self-injuries such as gunshot wounds and apparent suicide attempts. Patients usually did not remember these events. The underlying mechanisms by which these insomnia medicines cause complex sleep behaviors are not completely understood.

Please refer to the following website in FDA for details:
https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-risk-serious-injuries-caused-sleepwalking-certain-prescription-insomnia

In Hong Kong, there are 18 registered pharmaceutical products containing zolpidem, and all products are prescription-only medicines. There is no registered pharmaceutical product containing eszopiclone or zaleplon. So far, the Department of Health (DH) has received 3 cases of adverse drug reaction related to zolpidem, but these cases are not related to sleepwalking. The DH has not received any case of adverse drug reaction related to eszopiclone or zaleplon. News related to the safety of zolpidem, including risk of complex sleep behaviours, was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 2007, with the latest update posted on 16 May 2018. Letters to inform local healthcare professionals were issued by the DH on 6 Dec 2011 and 11 Jan 2013. In light of the above FDA's announcement on the new contraindication, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)