

# RGH Pharmacy E-Bulletin

Volume 33 (1): February 9, 2009

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH

© Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia 5041

## Parasomnias and psychiatric adverse effects with zolpidem

The term *parasomnia* is used in the Diagnostic and Statistical Manual of Mental Disorders (DSM) to refer to disorders involving abnormal behavioural or physiological events occurring in association with sleep, specific sleep stages, or sleep-wake transitions. Parasomnias do not involve problems with falling asleep, with or the timing of sleep and wakefulness, but do involve activation of the autonomic nervous system or cognitive processes during sleep or sleep-wake transitions. People affected by parasomnias usually have unusual behaviour during sleep rather than complaints of insomnia or excessive daytime sleepiness. Examples of parasomnias include nightmare disorder, sleep terror disorder, and sleep-walking.

Many medications have been associated with abnormal dreams and also unusual behaviour during sleep: in Australia, there has been considerable media focus and also attention amongst clinicians in relation to the effects of the hypnotic agent zolpidem (marketed in Australia as Stilnox<sup>®</sup>, Stildem<sup>®</sup>, GenRx zolpidem<sup>®</sup> (and many others) and elsewhere as Ambien<sup>®</sup>). The Approved Product Information issued by the manufacturers of Stilnox<sup>®</sup> tablets (Sanofi Aventis) specifically mentions a range of psychiatric and paradoxical reactions. These include “acute rage, restlessness, insomnia, agitation, irritability, aggression, delusions, anger, nightmares, hallucinations, abnormal behaviour and adverse behavioural affects.”

Zolpidem has been associated with other abnormal sleep-related behaviour that would be regarded as parasomnias. Examples of parasomnias that have been observed in patients treated with zolpidem include sleep-driving, eating during sleep, making telephone calls during sleep or even having sex during sleep without awareness. Sometimes patients who experience these parasomnias have amnesia for the event (they are unable to recall the event during subsequent enquiry). The product information further states that alcohol and other central nervous system depressants may have an additive effect thereby increasing the likelihood of somnambulism, parasomnias or bizarre behaviours during sleep. In other drug information resources there is further discussion of the adverse psychiatric effects of zolpidem. Hallucinations, fatigue, disturbance in attention, hypoesthesia and psychomotor retardation have each been reported in 2 - 4% of adults receiving recommended doses of zolpidem extended-release tablets. Appetite disorder, binge eating, paraesthesia, depersonalisation, disinhibition, mood swings and stress symptoms occurred in 1% of adults receiving recommended doses of zolpidem. Psychotic reactions have also been reported with zolpidem. In a discussion of the effects of zolpidem on memory, one study found that on the day following the administration of 10 mg and 20 mg doses of zolpidem, substantial memory loss was reported regarding the information presented to subjects during the periods of the maximum sedative effects associated with the drug (that is to say in the 90 minutes after the administration of the drug). There is also subjective evidence for anterograde amnesia occurring in association with zolpidem.

The Australian Adverse Drug Reaction Advisory Committee (ADRAC) holds details of various adverse reactions to zolpidem. As of early October 2008, ADRAC held details of 391 reports of the adverse reaction described as “amnesia,” including 322 cases where zolpidem was the sole agent implicated/suspected. With respect to psychiatric adverse reactions associated with zolpidem the ADRAC report describes many relevant cases, including the categories of “confusional state” (66 cases), “delirium” (13), “depersonalisation” (15), “hallucinations” (164), “paranoia” (13), “intentional drug misuse” (6), “psychotic disorder” (12) and “impulsive behaviour” (2). Other reports include “abnormal dreams” (10), “abnormal sleep-related event” (300), “sleep-related eating disorder” (15), somnambulism (218) and others. Clearly, caution is warranted where zolpidem is prescribed – long term treatment is not recommended.

Acknowledgment – This E-Bulletin is based on work by Chris Alderman, Senior Clinical Pharmacist, RGH

**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@rgh.sa.gov.au](mailto:chris.alderman@rgh.sa.gov.au)**  
Information in this E-Bulletin is derived from critical analysis of available evidence – individual clinical circumstances should be considered when making treatment decisions. You are welcome to forward this E-bulletin by email to others you might feel would be interested, or to print the E-Bulletin for wider distribution. Reproduction of this material is permissible for purposes of individual study or research.