

Zolpidem and Driving – A Dangerous Mix

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Numerous indicators show prescription drug abuse is a significant problem in the United States. According to the National Survey on Drug Use and Health (NSDUH), conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), in 2006 approximately 7 million persons 12 and older took a psychotherapeutic drug for non-medical purposes in the 30 days prior to the survey. Young adults (ages 18-25) by far showed the greatest use overall and the largest increases in past month, past year, and lifetime use between 2002 and 2006, compared to all other age groups (NSDUH, 2007).

At the same time, prescription drug abuse has become a serious threat to public health and safety, with unintentional deaths involving prescription opioids increasing 114 percent from 2001 to 2005, and treatment admissions increasing 74 percent in a similar four-year period (1). In 2006, the last year for which data are available, drug-induced deaths exceeded firearm-injury deaths and ranked second only to motor vehicle crashes as a cause of death (2).

The increase in prescription drug abuse is also having its effects on our nation's roadways. On July 13, 2009, the U.S. Department of Transportation's National Highway Traffic Safety Administration (NHTSA) released a report on the 2007 National Roadside Survey on Alcohol and Drug Use by Drivers (3). In a random sample of weekend nighttime drivers across the contiguous 48 states, researchers found that 16.3 percent of the drivers tested positive for drugs, compared to 2.2 percent of drivers with blood alcohol concentrations (BAC) at or above 0.08 g/dL. This was the first national study of roadside testing for drugs in addition to alcohol. The study found that drugs were present more than seven times as frequently as alcohol of those surveyed.

Law enforcement officers, prosecutors and toxicologists are also encountering an increase in impaired driving cases involving a variety of prescription drugs. One drug from the CNS depressant category having an impact on roadway safety is zolpidem, brand name Ambien®. The presence zolpidem became such a concern that impaired driving cases were studied in several states. (Washington: "*Zolpidem and Driving Impairment, 2001*" by Logan and Couper; and Wisconsin: "*Ambien -Drives Like a Dream? Case Studies of Zolpidem Impaired Drivers in Wisconsin*" by Liddicoat and Harding).

In the Washington study, state toxicologists at the Washington State Patrol's Bureau of Forensic Laboratory Services identified 29 impaired cases between January 1997 and December 1999 in which zolpidem was identified in the subjects' blood. In five of the cases, zolpidem was the only drug identified in the blood samples. The researchers concluded that it was reasonable to conclude that zolpidem has the potential to affect driving in a negative way (4).

The effect of zolpidem on driving ability was also examined, in part, in a double-blind, placebo-controlled, crossover study of 16 healthy volunteers (mean age 24.5 years). In the study a 10-mg dose of zolpidem was given at 11 pm. The next morning, one group of subjects was assessed in a driving simulator at 9 am and another group at 11 am; however, according to the researchers, zolpidem had no effect on driving ability at either time tested (*Psychopharmacology* 1999;143:373-9).

In another study with different results, investigators tried to determine the effect of middle-of-the-night administration of zolpidem on driving ability. Thirty volunteers participated in a double-blind study to measure the effects of zolpidem (10 or 20 mg) or a placebo four hours after administration. The test subjects drove a designated distance at a constant speed. A standard deviation of lateral position (drift) was the primary performance parameter. According to the findings, a 10 mg dose of zolpidem had a small effect while 20 mg significantly impaired driving (*J. Clin. Psychopharmacol*, 2002;22:576-83).

Zolpidem is a white to off-white crystalline powder. It is available by prescription only and is a Schedule IV controlled substance. Ambien® is available in strengths of 5 mg and 10 mg (white and pink oval tablets, respectively). Sonata® contains zaleplon. Imovane® and Lunesta® contain zopiclone. Zolpidem and the other sleep drugs are a non-benzodiazepine sedative-hypnotic, CNS depressant, sleep aid. Zolpidem is used in short-term treatment of insomnia. Zaleplon and zopiclone also are prescribed for the treatment of insomnia (5).

The recommended zolpidem dose is 10 mg immediately before bedtime (5 mg in the elderly). Recommended nighttime zaleplon and zopiclone doses are 5-20 mg and 7.5 mg, respectively. Patients treated with zolpidem often use other medications such as antidepressants, narcotic analgesics, and muscle relaxants, which can create additional problems if not used carefully.

Zolpidem goes by many different brand names in the U.S. and abroad, including Ambien, Zolpimist, Adormix, AmbienCR, Edluar, Damixan, Hypnogen, Myslee, Nytamel, Sanval, Stilnoct, Stilnox CR, Sucedal, Zoldmen, Zolnod and Zolpихexal. (Wikipedia)

Zolpidem and other similar sleep drugs act on the GABAA receptor, leading to central nervous system (CNS) depression. For this reason, users are cautioned to avoid operating heavy machinery or automobiles following zolpidem administration. Driving impairment caused by zolpidem is similar to that of ethanol and other CNS depressants, with adverse effects on vision, speech, balance and coordination. Notable symptoms of zolpidem impairment may include a glassy stare, extremely poor balance with noted sway, disorientation, slow and raspy speech, and memory impairment. The manufacturer of zolpidem states that patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motor coordination such as driving a motor vehicle.

To determine what effects might actually be observed in persons arrested for impaired driving associated with zolpidem, 28 actual impaired driving cases involving the use of zolpidem were reviewed using drug influence evaluation reports by drug recognition experts (DREs). The cases were examined to determine (1) the cause of the stop and arrest, (2) performance on the psychophysical tests administered during the DRE evaluation, (3) results of the eye

examinations, including horizontal gaze nystagmus (HGN), vertical gaze nystagmus (VGN), lack of convergence (LOC), and (4) vital signs including pulse rate, blood pressure, and body temperature.

In 27 of the 28 cases, blood samples were drawn and analyzed for the presence of drugs. In each case, the only drug detected was zolpidem. The zolpidem concentrations ranged from 0.05 to 0.69 mg/L with a mean of 0.22 mg/L. In one case, a zolpidem prescribed volunteer was examined by DREs for training purposes and no toxicology was obtained. None of the 28 cases involved the use of alcohol and in each case where a blood sample was obtained tests were negative for drugs other than zolpidem.

Overview of the 28 Case Zolpidem Study

The following chart represents information collected from the 28 actual zolpidem cases where the drivers were evaluated by a drug recognition expert (DRE). The information includes the cause of the stop/arrest, the suspect's performance on the psychophysical tests administered during the DRE evaluation; results of the eye examinations, including horizontal gaze nystagmus (HGN), vertical gaze nystagmus (VGN), lack of convergence (LOC); the suspect's vital signs including pulse rate; blood pressure, and body temperature.

Participants:	28 total	11 males	17 females
Ages:	Mean – 45	Range – 21 to 79 years	
Stop/Arrest:	Crash – 13	Other – 15 (weaving, fail to maintain single lane, disobeyed traffic signal, etc)	
Psychophysical tests: (Romberg balance Walk & Turn, One Leg Stand, Finger-to-nose)		Stopped: (safety reasons) – 7	Completed w/ difficulty: (5-8 clues) – 21
Eye Examinations:	HGN: 6 clues – 21 4 clues – 5 2 clues – 2	VGN: 13	Angle of onset: 30° – 12 35 – 40° – 7
Pupil sizes:	Room Light: Range: 2.0–7.0 Mean: 5.0 mm	NTD: Range 3.0–9.5 Mean: 7.0 mm	Direct Light: Range: 2.0–7.0 Mean: 4.5 mm
Vital Signs: Pulse Rate	1 st pulse: Range: 60–118 Mean: 90 bpm	2 nd pulse: Range: 60–120 Mean: 90 bpm	3 rd pulse: Range: 56–116 Mean: 86 bpm
Vital Signs: B/P and Temperature	Systolic: Range: 88 – 178 Mean: 132	Diastolic: Range: 58 – 110 Mean: 84	Body temperature: Range: 95.4 – 101.2 Mean: 97.0
Internal clock: (Romberg balance)	Range: 15 – 45 seconds Mean: 39 seconds		

Conclusion

Zolpidem and other similar hypnotics act as sleep inducers. The known and well-documented relationship between fatigue, sleepiness, and driving performance make zolpidem and other similar hypnotics potentially hazardous when used in close proximity to operating a motor vehicle. Based upon past studies addressing zolpidem and driving, and using the information collected from actual zolpidem impaired driving cases, it is reasonable to conclude that normal prescribed doses of zolpidem and similar hypnotics can adversely affect driving. It is also reasonable to conclude that when law enforcement officers encounter persons suspected of driving under the influence of zolpidem and similar hypnotics they may see a variety of impairment indicators that may or may not follow the “classic” or traditional CNS depressant signs and symptoms; however, some of the common indicators appear to be HGN, with an early angle of onset, a lack of convergence, and poor performance on the psychophysical tests.

Sources:

1. “National Prescription Drug Threat Assessment, 2009.”
2. Office of National Drug Control Policy News Release May 20, 2009.
3. Richard Compton and Amy Berning, Results of the 2007 National Survey of Alcohol and Drug Use by Drivers, NHTSA Facts, Washington DC; July 2009, DOT HS 811.
4. Zolpidem and Driving Impairment, Logan and Couper, J. Forensic Science, 2001.
5. Drugs and Human Performance Fact Sheets, NHTSA, DOT HS 809 725.