

The DAWN Report

August 7, 2014

Emergency Department Visits Attributed to Overmedication That Involved the Insomnia Medication Zolpidem

Zolpidem is a medication approved by the Food and Drug Administration (FDA) for short-term treatment of insomnia and is the active ingredient in the popular sleep aids Ambien®, Ambien CR®, Edluar®, and Zolpimist®.^{1,2,3,4} In 2010, approximately one third or 20,793 of the 64,175 emergency department (ED) visits involving zolpidem resulted from overmedication. This report examines zolpidem involvement in ED visits that are related to overmedication, which may occur when a patient takes too much of their own medications (i.e., exceeds the prescribed or recommended dose). Overmedication visits may involve multiple medications, but this analysis excludes visits that involved an illicit drug or prescription medications that were not prescribed for the patient or that were the result of a drug-related suicide attempt. All drugs involved in visits attributed to overmedication are documented; however, for visits involving multiple pharmaceuticals, it is not known which specific drug or drugs were taken in excess.

Even when taking the recommended dose of zolpidem, some patients find restful sleep difficult to achieve. When sleep does not come easily or is interrupted, patients may take more of their zolpidem medication than is prescribed. This may occur even though the medication guides for each zolpidem product mentioned above contain clear instructions to the patient to take the product exactly as prescribed.^{1,2,3,4,5,6}

Tracking ED visits involving zolpidem can help health professionals and patients understand the health consequences of overmedication associated with this drug and to consider appropriate safeguards and instructions to patients. The Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related ED visits in the United States. To be a DAWN case, an ED visit must have involved a drug, either as the direct cause of the visit or as a contributing factor. Data are collected on numerous illicit drugs, including cocaine, marijuana, heroin, and stimulants (e.g., amphetamines and methamphetamines), as well as pharmaceutical products, such as prescribed and over-the-counter medications. Data are



IN BRIEF

The total estimated number of zolpidem-related emergency department (ED) visits involving overmedication increased for both males and females between 2005-2006 and 2009-2010.

In 2010, females accounted for two thirds (68 percent) of zolpidem-related ED visits involving overmedication; patients aged 45 to 54 represented the largest proportion of zolpidem-related ED visits involving overmedication.

More than half of zolpidem-related ED visits involving overmedication in 2010 included other pharmaceuticals combined with zolpidem (57 percent).

Nearly half (47 percent) of zolpidem-related ED visits involving overmedication resulted in either a hospital admission or transfer in 2010, 26 percent of which were admissions to a critical or intensive care unit.

also collected for visits involving alcohol combined with other drugs and, for patients aged 20 or younger, alcohol when it is the only substance involved in the visit. A previous issue of *The DAWN Report* described zolpidem visits involving adverse reactions; this report describes visits involving overmedication.⁷ Overmedication, as defined in DAWN, includes only ED visits for patients who took medications prescribed or recommended for them and excludes patients who took a prescription drug not intended for them. Overmedication visits are those in which it was documented that more than the prescribed or recommended dose of an over-the-counter pharmaceutical, a dietary supplement, or a medication prescribed or recommended for that person had been taken. A visit is not included in this category if an illicit drug was involved or if the visit involved a suicide attempt.

To increase analytic capability and statistical power, this issue of *The DAWN Report* adds estimates together in two-year increments (i.e., 2005-2006, 2007-2008, and 2009-2010) within the Trends and Demographic

Characteristics sections. The remaining two sections of the report (Drug Combinations and Disposition) present detailed findings from 2010 only.

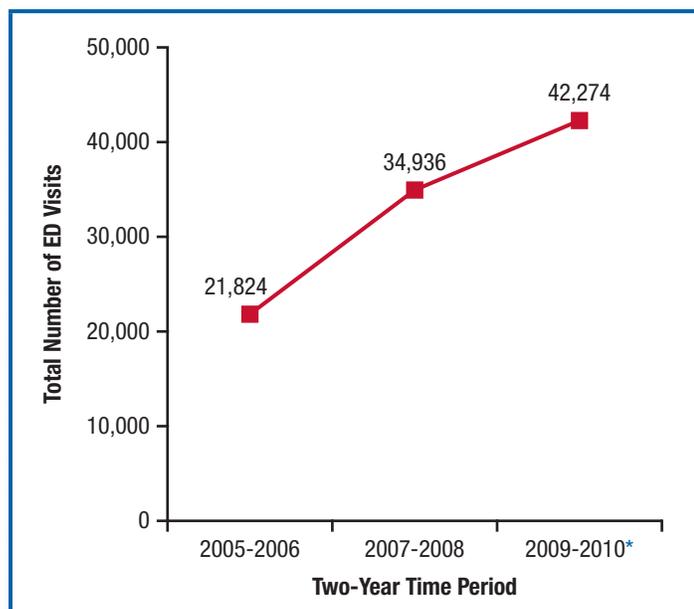
Trends in ED Visits

In 2005 and 2006, there was an estimated total of 21,824 zolpidem-related ED visits involving overmedication (Figure 1). Later, visits in 2009 and 2010 summed to about twice that number of visits (42,274 visits).

Demographic Characteristics

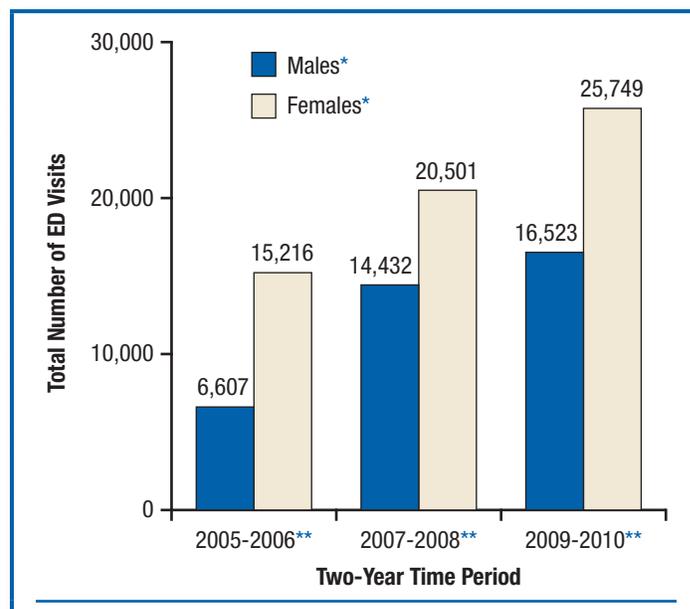
The total estimated number of zolpidem-related ED visits involving overmedication increased for both males and females between 2005-2006 and 2009-2010 (Figure 2). Overall, visits increased 150 percent among males (from a total of 6,607 visits in 2005 and 2006 to a total of 16,523 visits in 2009 and 2010) and by 69 percent among females (from a total of 15,216 visits in 2005 and 2006 to a total of 25,749 visits in 2009 and 2010) (Figure 2).

Figure 1. Zolpidem-Related Emergency Department (ED) Visits Involving Overmedication: Two-Year Combined Total Visits for 2005-2006, 2007-2008, and 2009-2010



*The difference between 2005-2006 and 2009-2010 is statistically significant at the .05 level.
Source: 2005 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Figure 2. Zolpidem-Related Emergency Department (ED) Visits Involving Overmedication, by Gender: Two-Year Combined Total Visits for 2005-2006, 2007-2008, and 2009-2010



*The difference between 2005-2006 and 2009-2010 is statistically significant at the .05 level.
**The difference between males and females is statistically significant at the .05 level.
Source: 2005 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

The following sections of this report will focus on the estimated 20,793 zolpidem-related visits attributed to overmedication that occurred in 2010, two thirds of which were made by females (68 percent). Patients aged 45 to 54 represented nearly one in three of these visits (31 percent) (Figure 3), and about one in five were aged 34 years or younger (4,831 visits, or 23 percent). An additional one in five were aged 35 to 44 years (4,468 visits, or 21 percent), and the remainder were either aged 55 to 64 (14 percent) or 65 or older (11 percent).

Drug Combinations Involved in ED Visits

Among zolpidem-related ED visits involving overmedication in 2010, 37 percent involved zolpidem only, accounting for an estimated 7,760 visits (Table 1). More than half of visits (57 percent) involved other pharmaceuticals combined with zolpidem. These included visits involving other anti-anxiety and insomnia medications (including benzodiazepines), accounting for an estimated 6,018 visits (29 percent),

Figure 3. Age Distribution among Zolpidem-Related Emergency Department (ED) Visits Involving Overmedication: 2010

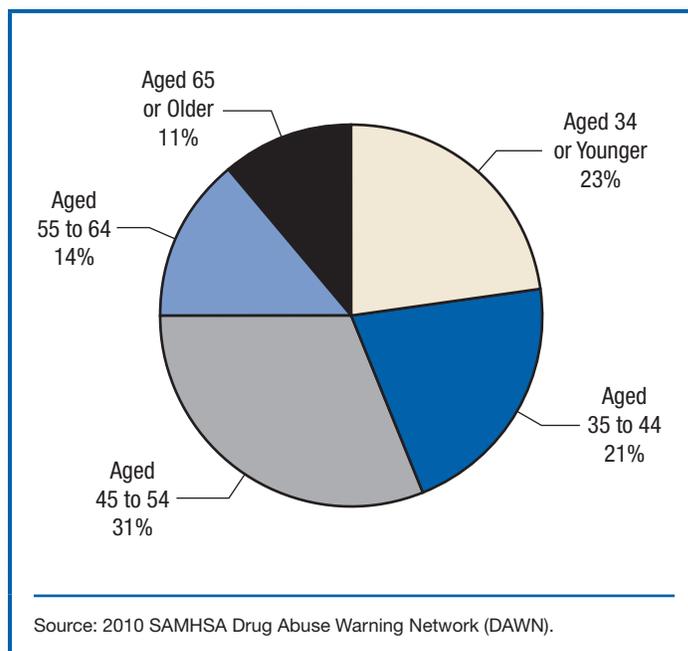


Table 1. Selected Drug Combinations for Zolpidem-Related Emergency Department (ED) Visits Involving Overmedication, All Visits Compared with Visits Resulting in Admission or Transfer: 2010

Drug Category/Combination	All ED Visits*: Number	All ED Visits*: Percent	ED Visits Resulting in Admission or Transfer*: Number	ED Visits Resulting in Admission or Transfer*: Percent
Total ED Visits	20,793	100	9,798	100
Zolpidem Only	7,760	37	2,901	30
Zolpidem in Combination with Other Pharmaceuticals	11,822	57	6,525	67
Pain Relievers	6,267	30	3,459	35
Narcotic Pain Relievers	5,217	25	2,694	28
Hydrocodone Combinations	1,930	9	863	9
Oxycodone Combinations	1,391	7	1,167	12
Other Anti-anxiety and Insomnia Medications	6,018	29	3,122	32
Benzodiazepines	5,479	26	2,832	29
Antidepressants	3,877	19	2,810	29
Antipsychotics	2,899	14	1,779	18
Muscle Relaxants	2,631	13	1,302	13
Anticonvulsants	1,479	7	1,227	13
Cardiovascular Medications	735	4	335	3
Zolpidem in Combination with Alcohol	2,851	14	1,267	13

*Because multiple drugs may be involved in each visit, estimates of visits by drug may add to more than the total, and percentages may add to more than 100 percent. Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

and those involving narcotic pain relievers, accounting for an estimated 5,217 visits (25 percent). In addition, 14 percent of visits involved alcohol combined with zolpidem (2,851 visits).

Disposition of ED Visits

Nearly half (47 percent) of zolpidem-related ED visits involving overmedication resulted in either a hospital admission or transfer (9,798 visits). This number includes an estimated 2,501 visits (26 percent) that resulted in admission to a critical or intensive care unit (ICU), with 1,253 (50 percent) of these ICU admissions involving medications that are also central nervous system (CNS) depressants: pain relievers or anti-anxiety and insomnia medications (data not shown).

Among zolpidem-related ED visits involving overmedication that resulted in hospital admission or transfer, 30 percent involved zolpidem only, whereas 67 percent of visits involved zolpidem in combination with other pharmaceuticals (Table 1). Approximately one third of visits that resulted in hospital admission or transfer (32 percent) involved other anti-anxiety and insomnia medications (3,122 visits), and 28 percent of visits involved narcotic pain relievers (2,694 visits). About 13 percent involved alcohol combined with zolpidem (1,267 visits).

Discussion

An estimated 50 to 70 million Americans suffer from chronic sleep disorders, which can affect performance on daily tasks and lead to negative health consequences.⁸ Zolpidem is a widely prescribed medication approved by the FDA for the short-term treatment of insomnia, but doses in excess of prescribed amounts led to an increasing number of ED visits since 2005. In 2013, the FDA issued a safety announcement “warning that patients who take the sleep medication zolpidem extended-release (Ambien CR)—either 6.25 mg or 12.5 mg—should not drive or engage in other activities that require complete mental alertness the day after taking the drug because zolpidem levels can remain high enough the next day to impair these activities.”⁹ The FDA also noted that “women appear to be more susceptible to this risk because they eliminate zolpidem from their bodies more slowly than men.”⁵ This FDA safety announcement required manufacturers to lower

the recommended dose of most zolpidem-containing medications by half for females. Similar action was recommended, although not required, for males.⁵

Researchers previously found that use of zolpidem in combination with other pharmaceuticals or alcohol was associated with increased likelihood of being admitted or transferred to the ICU.¹⁰ Findings in this report show that almost half of zolpidem-related ED visits involving overmedication resulted in hospital admission or transfer. More than two thirds of ED visits that resulted in hospital admission or transfer involved other pharmaceuticals, mostly other CNS depressant medications. CNS depression is the result of decreased brain activity, which may be caused by taking one or several CNS depressant medications and/or alcohol in combination that may then have cumulative depressant effects on the brain.¹⁰ These depressant effects include a decreased breathing rate, decreased heart rate, and loss of consciousness, possibly leading to coma or death.

The age distribution for zolpidem-related visits involving overmedication contrasts with the age distribution for those visits involving adverse reactions, as described in a previous issue of *The DAWN Report*.⁷ Although visits involving adverse reactions were more common among older age groups, visits involving overmedication were distributed more evenly across all age groups. Adults of all ages can help prevent overmedication by closely following the instructions for when and how to take all medications. If symptoms persist when the recommended amount of zolpidem is taken, patients should consult their prescribing physician. Health professionals can warn patients never to exceed the recommended dose unless told to do so by the prescriber.

These data, which focus on zolpidem overmedication ED visits and include only patients who were taking medications prescribed or recommended for them, underscore the importance of continued surveillance for overmedication of all drugs to evaluate drug safety. Enhancing drug safety is an important step toward improving public health and reducing health care costs. Pharmacists can serve as a source of safety information, especially for patients taking other prescription medications, including drugs that treat pain or anxiety, that may interact with zolpidem.^{6,11}

End Notes

1. Sanofi-Aventis. (2013). *Medication guide: Ambien*[®]. Retrieved from <http://www.fda.gov/downloads/drugs/drugsafety/ucm085906.pdf>
2. Sanofi-Aventis. (2013). *Medication guide: Ambien CR*[®]. Retrieved from <http://www.fda.gov/downloads/drugs/drugsafety/ucm085908.pdf>
3. Meda Pharmaceuticals. (2013). *Medication guide: Edluar*[®]. Retrieved from <http://www.fda.gov/downloads/drugs/drugsafety/ucm135937.pdf>
4. NovaDel Pharma Inc. (2008). *Medication guide: Zolpimist oral spray C-IV*. Retrieved from <http://www.fda.gov/downloads/drugs/drugsafety/ucm143465.pdf>
5. Food and Drug Administration. (2013). *FDA drug safety communication: Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem (Ambien, Ambien CR, Edluar, and Zolpimist)*. Retrieved from <http://www.fda.gov/drugs/drugsafety/ucm334033.htm>
6. National Library of Medicine. (2013). *Zolpidem: MedlinePlus drug information*. Retrieved from <http://www.nlm.nih.gov/medlineplus/druginfo/meds/a693025.html>
7. Center for Behavioral Health Statistics and Quality. (2013, May 1). *The DAWN Report: Emergency department visits for adverse reactions involving the insomnia medication zolpidem*. Rockville, MD: Substance Abuse and Mental Health Services Administration.
8. Institute of Medicine. (2006). *Sleep disorders and sleep deprivation: An unmet public health problem*. Washington, DC: The National Academies Press.
9. U.S. Food and Drug Administration. (2013). *FDA drug safety communication: FDA approves new label changes and dosing for zolpidem products and a recommendation to avoid driving the day after using Ambien CR*. Retrieved from <http://www.fda.gov/drugs/drugsafety/ucm352085.htm>
10. Zosel, A, Osterberg, E. C., & Mycyk, M. B. (2011). Zolpidem misuse with other medications or alcohol frequently results in intensive care unit admission. *American Journal of Therapeutics*, 18(4), 305-308.
11. Van Grootheest, A. C., & De Jong-van den Berg, L. T. W. (2005). The role of hospital and community pharmacists in pharmacovigilance. *Research in Social and Administrative Pharmacy*, 1(1), 126-133.

Suggested Citation

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The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA's mission is to reduce the impact of substance abuse and mental illness on America's communities.

The Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related morbidity and mortality. DAWN uses a probability sample of hospitals to produce estimates of drug-related emergency department (ED) visits for the United States and selected metropolitan areas annually. DAWN also produces annual profiles of drug-related deaths reviewed by medical examiners or coroners in selected metropolitan areas and States.

Any ED visit related to recent drug use is included in DAWN. All types of drugs—licit and illicit—are covered. Alcohol involvement is documented for patients of all ages if it occurs with another drug. Alcohol is considered an illicit drug for patients under age 21 and is documented even if no other drug is involved. The classification of drugs used in DAWN is derived from the *Multum Lexicon*, copyright 2012 Lexi-Comp, Inc., and/or Cerner Multum, Inc. The Multum Licensing Agreement governing use of the *Lexicon* can be found at <http://www.samhsa.gov/data/DAWN.aspx>.

DAWN is one of three major surveys conducted by SAMHSA's Center for Behavioral Health Statistics and Quality (CBHSQ). For more information on other CBHSQ surveys, go to <http://www.samhsa.gov/data/>. SAMHSA has contracts with Westat (Rockville, MD) and RTI International (Research Triangle Park, NC) to operate the DAWN system and produce publications.

For publications and additional information about DAWN, go to <http://www.samhsa.gov/data/DAWN.aspx>.



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