Albert Einstein Medical Center
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December 23rd, 2008

Albert Einstein Healthcare Network

Albert Einstein Medical Center

Belmont Behavioral Health

Germantown Community Health Services

MossRehab

Willowcrest

Willow Terrace

Mr. Michael S. Peasley
Peasley and Peasley Investigations
FAX (727) 461-4359

Mr. Peasley,

Thank you for the opportunity to be of service during your investigation of the death of Laura Bowdoin. I have FAXed to your office my three page report on zolpidem (Ambien®). I have tried to work as quickly as possible to prepare the report. It is complete and extensively referenced as per my understanding of the assignment. If this report is not what you had in mind when we discussed the assignment last week, please let me know and I will make every effort to satisfy the needs of your investigation.

Please remit $500, as agreed, to the following address: Gerald F. O'Malley, 880 Weikel Road, Lansdale, PA 19446 for services rendered.

19446

Cordially,

Gerald F. O'Malley, DO

Report on the Potential for Lethality of Zolpidem with Comments on the Contribution of Zolpidem to the Death of Laura Bowdoin

Zolpidem is a sedative hypnotic medication approved by the FDA in December 1992 for the treatment of insomnia. Since its introduction to the market, zolpidem has become the most widely prescribed sleep aid in the United States.[1] Over 25,000,000 prescriptions for Zolpidem were written in 2006[2] and many more are expected to be written in the future since the drug was approved for generic formulation in April 2007[3] and overall use of zolpidem has increased 15% from December 1 2004 – November 30th 2007.[4] Given the tremendous use of the drug, the expectation is that some people will abuse zolpidem for a variety of reasons; some accidental and some intentional. What is remarkable is that given the widespread availability and utilization of zolpidem it remains a very safe drug, even in overdose. Given the number of prescriptions written there are very few cases of death or serious morbidity associated with zolpidem (see Table 1).[4]

Table 1. Adverse Event Reports since Market Approval of Ambien® (zolpidem) December 16, 1992 – November 30th 2007

Crude counts*	All Reports	Serious	Death
Unknown Age	1810 (1693)	885 (769)	98 (86)
Pediatrics (0-16)	134 (77)	107 (57)	15 (11)
Adults (>17)	4872 (3270)	3831 (2346)	697 (591)
All ages	6816 (5040)	4823 (3172)	810 (688)

*Includes duplicates and unknown ages
**Serious AEs per regulatory definition (CFR 314.80) include death, lifethreatening, hospitalization (initial or prolonged), disability & congenital

In European postmarketing surveillance of overdose with zolpidem alone, most adverse events reports describe impairment of consciousness ranging from somnolence to light coma. There was one case each of cardiovascular and respiratory compromise. Individuals have fully recovered from zolpidem tartrate overdoses up to 400 mg (40 times the maximum recommended dose). Overdose cases involving multiple CNS-depressant agents, including zolpidem, have resulted in more severe symptomatology, including fatal outcomes.[5]

The cases of zolpidem overdose that have resulted in death and published in the medical literature are rare. Most of the cases described in the medical and forensics literature have reported postmortem zolpidem levels in the range of 1 to 4 mg/L (see Table 2).[6-12]

Table 2. Summary of Deaths Associated with Zolpidem Reported in the Medical and Forensics Literature

Reference	Number of Cases	Outcome	Zolpidem Level	Co-Ingestants
Traqui 1993	1	Death	3.29mg/L (blood)	Acepromazine2.4mg/L
Khodasevitch 1996	1	Death	0.8mg/L (blood)	Ethanol 240mg/dL
Deveaux 1998	1	Death	0.9mg/L (blood)	Ethanol 250mg/dL
Bronstein 2007	1	Death	0.33mg/L (blood)	Oxycodone, tramadol, etodolac, ibuprofen

Bronstein 2007	1	Death	0.1mg/L (blood)	Oxycodone, acetaminophen / tramadol
Bronstein 2007	1	Death	0.6mg/L(blood)	Tramadol, meperidine, sertraline
Bronstein 2007	1	Death	0.1mg/L(blood)	Oxycodone, diazepam, antihistamine/decongestant, naproxen, amphetamine
Bronstein 2007	1	Death	0.1mg/L(blood)	Hydrocodone, tramadol, lisinopril, mirtazapine, meprobamate
Bronstein 2007	1	Death	8.4mg/L (blood)	Acetaminophen / diphenhydramine, alprazolam, risperidone, fluvoxamine
Bronstein 2007	1	Death	0.6mg/L (blood)	Methadone
Bronstein 2007	1	Death	0.58mg/L (serum)	Amitriptyline, nortriptyline
Bronstein 2007	1	Death	2.4mg/L (blood)	Promethazine
Bronstein 2007	1	Death	0.021mg/L (blood)	Quetiapine, ethanol
Bronstein 2007	1	Death	1.9mg/L (blood)	Acetaminophen / hydrocodone, propoxyphene, codeine
Baselt 2004	7	Death	Avg 2.8mg/L (blood) (range 1.1-4.5mg/L)	At least one (caffeine, risperidone, carbamazepine, naproxen)
Baselt 1996	1	Death	4.3mg/L (heart)	None
Lichtenwalner 1999	1	Death	7.9mg/L	None
Jung 2007	1	Survive	8.4mg/L (blood)	None

Every zolpidem-related fatality with post-mortem zolpidem levels reported by the American Association of Poison Control Centers from 2007 is reproduced in Table 2. Every zolpidem related death reported to the American Association of Poison Control Centers in 2007 involved a co-ingestant.[9]

The conclusion of the article by Jung from 2007 is "In conclusion our case supports the position of the long held view that Zolpidem single-drug poisonings are generally benign and could be survived in high doses with supportive care."[12] This conclusion is not an overstatement. Zolpidem as an isolated ingestion is very well tolerated even in massive quantities. Most of the cases described in the literature of death associated with zolpidem have occurred in the elderly or in patients that ingest several substances such as alcohol, tramadol, opiates such as methadone or another central nervous system depressant.

The subject of this report is the death of Laura Bowdoin in June 2008. The cause of death in the case of Ms. Bowdoin is listed on the autopsy report as being zolpidem toxicity. The level of zolpidem in Ms. Bowdoin's heart (0.93mg/L) at the time of her autopsy was actually very low compared with levels that have been reported in the medical and forensic literature. All of the cases that I am aware of that have postmortem zolpidem levels in a similar range to that of Ms. Bowdoin have had other co-ingestants in their

blood in addition to the zolpidem. Most of the zolpidem –related fatalities that have been reported have been elderly people with numerous medical problems putting them at higher risk for serious multi-organ system injury following an overdose and younger people with numerous co-ingestants, most commonly alcohol. Almost all the fatalities have had much higher postmortem zolpidem levels compared with Ms. Bowdoin.

Ms. Bowdoin was, by all reports, a very healthy individual with no medical problems and taking no medications. The levels of zolpidem in her body following her death were quite low compared with previously reported postmortem levels in cases of fatal overdose. Although it is possible that Ms. Bowdoin was killed by an overdose of zolpidem, given what is known and what has been published on the nature of zolpidem in overdose I think that it is improbable that the zolpidem alone caused Ms. Bowdoin's death. A description of the condition of her surroundings and environment in which she was found at the time of her death would be helpful in discerning if another explanation is more plausible or other elements contributed to Ms. Bowdoin's death.

References:

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