K51 Zolpidem Concentrations Found in 644 Blood Samples Submitted for Driving Under the Influence of Drugs (DUID) Analysis

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After attending this presentation, attendees will be better informed regarding zolpidem and the blood concentrations measured in a large population of drivers investigated for DUID.

This presentation will impact the forensic science community by providing additional information that may be of benefit to toxicologists, pathologists, and investigators when evaluating similar types of cases.

Zolpidem (Ambien®) is a sleep-aid classified as a non-benzodiazepine hypnotic of the imidazopyridine class that is prescribed for the short-term treatment of insomnia. Because of its sedative-hypnotic properties, the drug has often been implicated with impaired driving, drug-facilitated crimes, and lethal outcomes. Some common effects associated with zolpidem use include dizziness, headache, and nausea, while rare effects include somnambulism and anterograde amnesia. Cases have been reported in which people, after taking zolpidem, performed complex tasks such as eating, shopping, or driving, but then had little or no memory about the events after awakening. Due to the frequency of zolpidem use and its potential adverse effects profile, it is relevant to evaluate blood drug concentrations in drivers.

Over the course of an approximate 4-year period, 644 blood samples have been tested for zolpidem in specimens submitted for toxicology testing as part of the DUID investigation process. The test is briefly described as follows: blood samples underwent a four-fold dilution prior to mixing with a deuterated internal standard (zolpidem-d6) and 1% phosphoric acid. Zolpidem was then extracted through a solid phase extraction procedure. Eluents were evaporated to dryness, subsequently reconstituted with 50% Deionized (DI) water/50% Mobile Phase, and supernatants were centrifuged prior to transfer to autosampler vials. Analysis was achieved using reverse phase High-Performance Liquid Chromatography (HPLC) separation with positive-ion Electrospray Tandem Mass Spectrometry (ES/MS/MS) for detection and quantification. The ions monitored for zolpidem were 308.0m/z to 235.0m/z and 263.0 m/z, respectively. The lower limit of quantification was 4.0ng/mL with an analytical measurement range of 4.0ng/mL-800ng/mL.

A review of the data set revealed that these samples were positive across a wide concentration range (i.e., from less than 4.0ng/mL to 2,000ng/mL). The mean ± Standard Deviation (SD) and median from 636 positive results were 255ng/mL ± 286ng/mL and 150ng/mL, respectively. As a point of reference, plasma concentrations following single oral 5mg and 10mg doses occur at approximately 1.6hrs following ingestion and range from 29ng/mL to 113ng/mL for the 5mg dose and 58ng/mL to 272ng/mL for the 10mg dose. Most results are, therefore, consistent with therapeutic concentrations. The average age by gender was 44.7yrs (range: 21yrs-71yrs; median: 45yrs) for females (*n*=170), and 46.1yrs (range: 19yrs-87yrs; median: 46yrs) for males (*n*=201). In 2013, the Food and Drug Administration informed manufacturers that the recommended dose of zolpidem for women should be lowered from 10mg to 5mg for immediate-release products and from 12.5mg to 6.25mg for extended-release products. Differentiating this data by gender showed an average concentration in females (*n*=176) of 271ng/mL ± 300ng/mL (range, 5.6 g/mL-1,400ng/mL) with a median value of 155ng/mL. In males (*n*=201), the average concentration was 222ng/mL ± 245ng/mL (range, 4ng/mL-1,700ng/mL) with a median value of 140ng/mL. Of the 636 positive cases, 79 were positive for only zolpidem. In this subset of cases, the average concentration was 314ng/mL ± 321ng/mL (range, 5.9ng/mL-1,700ng/mL) with a median value of 200ng/mL. Other drugs identified in the entire population included amphetamines (e.g., methamphetamine), benzodiazepines (e.g., diazepam, alprazolam, clonazepam, and lorazepam), and opiates (e.g., oxycodone, hydrocodone, and fentanyl), among others.

This data demonstrates that zolpidem is associated with driving impairment across a wide concentration range. Because zolpidem is a sleep aid, concentrations consistent with therapeutic concentrations would not be considered compatible with the safe operation of a motor vehicle. Concentrations that are well above concentrations associated with prescribed dosages imply tolerance to the medication. Per research, these data represent the largest population of zolpidem positive specimens that has been evaluated in regard to the impaired operation of a motor vehicle.

Zolpidem, DUID, Impaired Driving

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