Zopiclone
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Zopiclone (brand name Zimovane in Europe and Imovane elsewhere) is a nonbenzodiazepine hypnotic agent used in the treatment of insomnia. It is a cyclopyrrolone, which increases the normal transmission of the neurotransmitter GABA in the central nervous system, as benzodiazepines do, but in a different way.

As zopiclone is sedating it is marketed as a sleeping pill. It works by causing a depression or tranquilization of the central nervous system. After prolonged use the body can become accustomed to the effects of zopiclone. When the dose is then reduced or the drug is stopped, withdrawal symptoms may result. These can include a range of symptoms similar to those of benzodiazepine withdrawal.

In the United States, zopiclone is not commercially available,[1] although its active stereoisomer, eszopiclone, is sold under the name Lunesta (see History). Zopiclone is a controlled substance in the United States, Japan, Brazil, and some European countries, and may be illegal to possess without a prescription.

Zopiclone is known colloquially as a "Z-drug." Other Z-drugs include zaleplon (Sonata) and zolpidem (Ambien and AmbienCR) and were initially thought to be less addictive and/or habit forming than benzodiazepines. However, this appraisal has shifted somewhat in the last few years as cases of addiction and habituation have been presented. It is recommended that zopiclone be taken on a short-term basis, usually a week or less.[2] Daily or continuous use of the drug is not usually advised.[3]

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Zopiclone

Systematic (IUPAC) name
(RS)-6-(5-chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazin-5-yl 4-methylpiperazine-1-carboxylate

Clinical data

Trade names Imovane, Zimovane
AHFS/Drugs.com International Drug Names

Pregnancy cat. AU: C
US: C

Legal status AU: Prescription Only (S4)
UK: POM
US: Schedule IV

Routes Oral tablets, 3.75mg (UK), 5 or 7.5 mg

Pharmacokinetic data
Bioavailability 52-59% bound to plasma protein
Metabolism Various cytochrome P450 liver enzymes
Half-life ~6 hours
~9 hours for over 65

Excretion Urine

Identifiers

CAS number

Medical uses

Zopiclone is indicated for the short term treatment of insomnia where sleep initiation or sleep maintenance are prominent symptoms. Long-term use is not recommended as tolerance, dependence and addiction can occur with prolonged use.[4][5]

Elderly

Zopiclone, similar to other benzodiazepines and nonbenzodiazepine hypnotic drugs causes impairments in body balance and standing steadiness in individuals who wake up at night or the next morning. Falls and hip fractures are frequently reported. The combination with alcohol consumption increases these impairments. Partial, but incomplete tolerance develops to these impairments.[6]

An extensive review of the medical literature regarding the management of insomnia and the elderly found that there is considerable evidence of the effectiveness and lasting benefits of nondrug treatments for insomnia. Compared with the benzodiazepines, the nonbenzodiazepine sedative-hypnotics, such as zopiclone, offer few if any advantages in efficacy or tolerability in elderly persons. It was found that newer agents such as the melatonin agonists may be more suitable and effective for the management of chronic insomnia in elderly people. Long-term use of sedative-hypnotics for insomnia lacks an evidence base and is discouraged for reasons that include concerns about such potential adverse drug effects as cognitive impairment (anterograde amnesia), daytime sedation, motor incoordination, and increased risk of motor vehicle accidents and falls. In addition, the effectiveness and safety of long-term use of nonbenzodiazepine hypnotic drugs remains to be determined. It was concluded that further research is needed to evaluate the long-term effects of treatment and the most appropriate management strategy for elderly persons with chronic insomnia.[7]

Adverse reactions
The side-effect most commonly seen in clinical trials is taste alteration or dysgeusia (bitter, metallic taste, which is usually fleeting in most users but can persist until the drug's half-life has expired). Palpitations may occur in the daytime following withdrawal from the drug after prolonged periods of use (especially when taken for more than two weeks).

Zopiclone induces amnesia type memory impairments similar to triazolam and Rohypnol. Impairment of driving skills with a resultant increased risk of road traffic accidents is probably the most important side effect. This side effect is not unique to zopiclone but also occurs with other hypnotic drugs. A study assessing the impact of zopiclone on driving skills the next day found that the impairments on driving skills are double that of a social dose of alcohol. Zaleplon had no detrimental effects on driving skills the next day. Daytime withdrawal related anxiety can also occur from chronic nightly nonbenzodiazepine hypnotic usage such as with zopiclone.

More common

Gastrointestinal: taste disturbances including bitter metallic taste, dry mouth. Nervous system: disruption of REM sleep, double vision, drowsiness, memory impairments, visuospatial impairments, dizziness, headaches, and fatigue. Unexpected mood changes have been noted, which if experienced should lead to the drug's being withdrawn from the patient.

Less common

- **Gastrointestinal**: heartburn, constipation, diarrhoea, nausea, coated tongue, bad breath, anorexia or increased appetite, vomiting, epigastric pains, dyspepsia, dehydration, parageusia.
- **Cardiovascular**: palpitations in elderly patients.
- **Skin**: urticaria, tingling in the arms and legs.
- **Miscellaneous**: blurred vision, frequent micturition, nocturnal enuresis, mild to moderate increases in serum transaminases and/or alkaline phosphatase and interstitial nephritis have been reported very rarely.
- **Reproductive**: impotence, delayed ejaculation, anorgasmia in both women and men.
- **Nervous system**: agitation, anxiety, loss of memory including retrograde and anterograde amnesia, confusion, dizziness, weakness, somnolence, asthenia, euphoria and/or dysphoria, feeling of drunkenness, depression, sleep walking, coordination abnormality, hypotonia, speech disorder, hallucinations of various strengths, usually auditory and visual, behavioural disorders, aggression, tremor, rebound insomnia, nightmares, hypomania. Delirium can also occur but is a side effect mainly seen in the elderly.

Tolerance, dependence and withdrawal

Zopiclone, a benzodiazepine-like drug was introduced and initially promoted as having less dependence and withdrawal than traditional benzodiazepine drugs. However, zopiclone may have an even greater addictive potential than benzodiazepines and has been described as a "benzodiazepine in disguise". Tolerance to the effects of zopiclone can develop after a few weeks. Long term use
should be avoided in most cases. Patients with severe insomnia resulting from anxiety can be successfully treated for months. Abrupt withdrawal particularly with prolonged and high doses can in severe cases cause seizures and delirium.\[30]\[31]

Publications in the *British Medical Journal* do not give any evidence to the claim that zopiclone has a low dependence potential. In fact, physical dependence and recreational abuse and withdrawal syndromes similar to those seen in benzodiazepine withdrawal are frequently encountered. Withdrawal symptoms included anxiety, tachycardia, tremor, sweats, flushes, palpitations, derealisation, and further insomnia.\[32]\ Suspected withdrawal convulsions during detoxification from zopiclone has been reported, however the individual was a high dose zopiclone misuser.\[33]\n
The risk of dependency on zopiclone when used for less than 2 weeks or only used occasionally is low.\[34]\ However, this is disputed by one study of low dose zopiclone taken for only 7 nights. It found that discontinuation of zopiclone caused significant rebound insomnia. Furthermore when midazolam taken for 7 nights was discontinued no rebound insomnia occurred suggesting that zopiclone may have even more significant problems of tolerance and dependence than the benzodiazepines.\[35]\ After 3 weeks of use mild to moderate rebound withdrawal symptoms appear upon discontinuation of zopiclone.\[36]\ Due to the risk of tolerance and physical dependence, zopiclone is only recommended for short term (1–4 weeks max) relief of insomnia, or alternatively, long term infrequent use.\[37]\ Long-term zopiclone users who have become physically dependent should not discontinue their medication abruptly as severe withdrawal symptoms may occur such as delirium.\[38]\ If zopiclone has been taken for more than a few weeks then the medication should be gradually reduced or preferably to cross over to an equivalent dose of diazepam (Valium), which has a much longer half-life, which makes withdrawal easier and then gradually taper their dosage over a period of several months in order to avoid extremely severe and unpleasant withdrawal symptoms (e.g., inner restlessness, psychomotor agitation, abdominal pain, hypertension, hallucinations, seizures, anxiety, depression, psychosis, etc.), which can last up to two years after withdrawal if the withdrawal is done too abruptly.\[39]\[40]\[41]\ After 4 weeks of nightly use of zopiclone day time withdrawal related anxiety begin to emerge in some users. However, the daytime withdrawal anxiety does not appear to be as intense as that seen with the much shorter-acting triazolam, which provokes even more profound daytime withdrawal anxiety symptoms in long-term users.\[42]\n
According to the World Health Organisation, zopiclone, although molecularly not a benzodiazepine, binds unselectively with high affinity to the same benzodiazepine sites that the benzodiazepine class of drugs do. The World Health Organisation also stated that zopiclone is cross tolerant with benzodiazepines and one can substitute one for the other. In the review of zopiclone by the World Health Organisation they found that the appearance of withdrawal symptoms usually occurred either when the drug was misused in excessive doses or when use of zopiclone was prolonged. The withdrawal symptoms from zopiclone reported included anxiety, tachycardia, tremor, sweating, rebound insomnia, derealisation, convulsions, palpitations and flushes.\[43]\n
Zopiclone is cross tolerant with benzodiazepines.\[44]\ Alcohol has cross tolerance with \(\text{GABA}_A\) receptor positive modulators such as the benzodiazepines and the nonbenzodiazepine drugs. For this reason alcoholics or recovering alcoholics may be at increased risk of physical dependence on zopiclone. Also, alcoholics and drug abusers may be at increased risk of abusing and or becoming psychologically dependent on zopiclone. Zopiclone should be avoided in those with a history of alcoholism, drug misuse (illicit or prescription misuse), or in those with history of physical dependency or psychological dependency on sedative-hypnotic drugs.
Withdrawing from Zopiclone sleeping tablets has been recommended to be done via a cross over to an equivalent dose of diazepam. This is because diazepam is available in low potency tablets, is cross-tolerant with zopiclone and is longer acting than zopiclone, which allows for a smoother withdrawal and for the body to adjust to a constant dose.\[45][46][47]\ While zopiclone acts on the same benzodiazepine receptors as the benzodiazepine family of drugs it is not classed as a benzodiazepine (with which it shares a number of characteristics and effects) due to its differing molecular structure. Zopiclone is classed as a cyclopyrrolone derivative.\[48]

**Carcinogenicity**

A recent analysis of both U.S. Food and Drug Administration (FDA) data and clinical trial data shows that nonbenzodiazepine Z-drugs at prescribed doses cause an increased risk of developing cancer in humans. There have been 15 epidemiological studies, which have shown that hypnotic drugs cause increased mortality, mainly due to increased cancer deaths. The cancers included those of the brain, lung, bowel, breast, and bladder. One possible explanation for the increased cancer deaths is that the Z-drugs have an adverse effect on the immune system. The fact that clinical trial subjects taking other Z-drugs (zolpidem, zaleplon and eszopiclone) had an increased rate of infections seems to support this theory. Benzodiazepine hypnotic agents are also associated with an increased risk of cancer in humans, namely ovarian cancer. Development of malignancy has been associated with zolpidem usage, but the incidence of neoplasm in zolpidem users is as yet unknown.\[49\]

Indiplon, another nonbenzodiazepine drug has also shown an increased rate of cancers in clinical trials. The review author concluded by saying: "The likelihood of cancer causation is sufficiently strong now that physicians and patients should be warned that hypnotics possibly place patients at higher risk for cancer".\[49\]

**Contraindications**

Zopiclone causes impaired driving skills that are similar to those of benzodiazepines. Long-term users of hypnotic drugs for sleep disorders develop only partial tolerance to adverse effects on driving with users of hypnotic drugs even after 1 year of use still showing an increased motor vehicle accident rate.\[50\] Patients who drive motor vehicles should not take zopiclone unless they stop driving due to a significant increased risk of road traffic accidents in zopiclone users.\[51\] Zopiclone induces impairment of psychomotor function.\[52][53\] Driving or operating machinery should be avoided after taking zopiclone as effects can carry over to the next day including impaired hand eye coordination.\[54][55\] Patients with a history of substance abuse should not be prescribed zopiclone, as it has a very high potential for problematic drug misuse.\[56\] Zopiclone is known to, in some case, induce a state of amnesia, which is largely related (and not very dissimilar) to 'sleep-walking'. This can extend to sleep-eating, sleep-talking (quite naturally), to dangerously 'sleep driving'. It is, therefore, usually not used as an anti-anxiety drug (such as Benzodiazepines), as the patients may be liable to make very poor judgment decisions (as they are, in essence, mentally 'asleep') and attempt dangerous activities, even with potentially no recollection of any of the events afterward.\[57\]

**Special precautions**

Alcohol should be avoided when using zopiclone, as alcohol and zopiclone enhance the effects of each other and the risk of dependence could increase.\[58\]
Patients with liver disease eliminate zopiclone much more slowly than normal patients and in addition experience exaggerated pharmacological effects of the drug.\[^{59}\]\n
Zopiclone increases sway and increases the number of falls in older people as well as cognitive side effects. Falls are a significant cause of death in older people.\[^{60}\][\(^{61}\)[\(^{62}\]\n
Patients who suffer from muscle weakness due to myasthenia gravis or have poor respiratory reserves due to severe chronic bronchitis, emphysema or other lung disease, or have sleep apnoea cannot safely take zopiclone, nor can a patient with any untreated abnormality of the thyroid gland.\[^{63}\]\n
### EEG and sleep

Similar to other sedative hypnotic drugs zopiclone causes a decrease in the core body temperature and is effective in decreasing sleep latency.\[^{64}\]\n
Zopiclone causes similar alterations on EEG readings and sleep architecture as benzodiazepines and causes disturbances in sleep architecture on withdrawal as part of its rebound effect.\[^{65}\][\(^{66}\]\n
Zopiclone reduces both delta waves and the number of high-amplitude delta waves whilst increasing low-amplitude waves.\[^{67}\]\n
Zopiclone reduces the total amount of time spent in REM sleep as well as delaying its onset.\[^{68}\][\(^{69}\]\n
Cognitive behavioral therapy has been found to be superior to zopiclone in the treatment of insomnia and has been found to have lasting effects on sleep quality for at least a year after therapy.\[^{70}\][\(^{71}\)[\(^{72}\][\(^{73}\]\n
### Pharmacology

The therapeutic pharmacological properties of zopiclone include hypnotic, anxiolytic, anticonvulsant, and myorelaxant properties.\[^{74}\]\n
Both zopiclone and benzodiazepines act indiscriminately at the benzodiazepine-binding site on α1, α2, α3, and α5 GABA\(_A\)-containing receptors as full agonists causing an enhancement of the actions of GABA to produce the therapeutic and adverse effects of zopiclone. The metabolite of zopiclone called desmethylzopiclone is also pharmacologically active, although it has predominately anxiolytic properties. Like benzodiazepines, zopiclone and its active metabolite desmethylzopiclone also inhibit N-methyl-D-aspartate (NMDA) receptors and nicotinic acetylcholine (nAChRs) receptors, which might play a role in the addictive properties of these drugs.\[^{75}\][\(^{76}\]\n
One study however, found some slight selectivity for zopiclone on α1 and α5 subunits.\[^{77}\]\n
Although it is regarded as being unselective in its binding to α1, α2, α3 and α5 GABA\(_A\) benzodiazepine receptor complexes. Desmethylzopiclone has been found to have partial agonist properties, unlike the parent drug zopiclone, which is a full agonist.\[^{78}\]\n
The mechanism of action of zopiclone is similar to benzodiazepines, with similar effects on locomotor activity and on dopamine and serotonin turnover.\[^{79}\][\(^{80}\]\n
A meta-analysis of randomised controlled clinical trials that compared benzodiazepines to zopiclone or other Z Drugs such as zolpidem and zaleplon has found that there are few clear and consistent differences between zopiclone and the benzodiazepines in terms of sleep onset latency, total sleep duration, number of awakenings, quality of sleep, adverse events, tolerance, rebound insomnia, and daytime alertness.\[^{81}\]\n
Zopiclone is in the cyclopyrrole family of drugs. Other cyclopyrrole drugs include suriclone. Zopiclone, although molecularly different from benzodiazepines, shares an almost identical pharmacological profile as benzodiazepines, including anxiolytic properties. Its mechanism of action is via binding to the benzodiazepine site and acting as a full agonist, which in turn positively modulates
benzodiazepine-sensitive GABA<sub>A</sub> receptors and enhances GABA binding at the GABA<sub>A</sub> receptors to produce zopiclone's pharmacological properties.\[82]\[83]\[84] In addition to zopiclone's benzodiazepine pharmacological properties, it also has some barbiturate-like properties.\[85]\[86]

In EEG studies, zopiclone significantly increases the energy of the beta frequency band and shows characteristics of high-voltage slow waves, desynchronization of hippocampal theta waves and an increase in the energy of the delta frequency band. Zopiclone increases both stage 2 and slow wave sleep (SWS), while zolpidem, an α1-selective compound, increases only SWS and causes no effect on stage 2 sleep. Zopiclone is less selective to the α1 site and has higher affinity to the α2 site than zaleplon. Zopiclone is therefore very similar pharmacologically to benzodiazepines.\[87]

### Pharmacokinetics

After oral administration, zopiclone is rapidly absorbed, with a bioavailability of approximately 80%. The plasma protein binding of zopiclone has been reported to be between 45 and 80%. Zopiclone is rapidly and widely distributed to body tissues including the brain, and is excreted in urine, saliva, and breast milk. Zopiclone is partly metabolised in the liver to form an inactive N-demethylated derivative and an active N-oxide metabolite. In addition, approximately 50% of the administered dose is decarboxylated and excreted via the lungs. In urine, the N-demethyl and N-oxide metabolites account for 30% of the initial dose. Between 7 and 10% of zopiclone is recovered from the urine, indicating extensive metabolism of the drug before excretion. The terminal elimination half-life (t1/2z) of zopiclone ranges from 3.5 to 6.5 hours. The pharmacokinetics of zopiclone in humans are stereoselective. After oral administration of the racemic mixture, Cmax (time to maximum plasma concentration), AUC (area under the plasma time-concentration curve) and t1/2z values are higher for the dextrorotatory enantiomer, owing to the slower total clearance and smaller volume of distribution (corrected by the bioavailability), compared with the levorotatory enantiomer. In urine, the concentrations of the dextrorotatory enantiomers of the N-demethyl and N-oxide metabolites are higher than those of the respective antipodes. The pharmacokinetics of zopiclone are altered by aging and are influenced by renal and hepatic functions.\[88]

### Interactions

Zopiclone also interacts with trimipramine and caffeine.\[89]\[90] Alcohol has an additive effect when combined with zopiclone, enhancing the adverse effects including the overdose potential of zopiclone significantly.\[91]\[92] Erythromycin appears to increase the absorption rate of zopiclone and prolong the elimination half-life of zopiclone, leading to increased plasma levels and more pronounced effects. Itraconazole has a similar effect on zopiclone pharmacokinetics as erythromycin. The elderly may be particularly sensitive to the erythromycin and itraconazole drug interaction with zopiclone. Temporary dosage reduction during combined therapy may be required, especially in the elderly.\[93]\[94] Rifampicin causes a very notable reduction in half-life of zopiclone and peak plasma levels, which results in a large reduction in the hypnotic effect of zopiclone. Phenytoin and carbamazepine may also provoke similar interactions.\[95] Ketoconazole and sulfaphenazole interfere with the metabolism of zopiclone.\[96] Nefazodone impairs the metabolism of zopiclone leading to increased zopiclone levels and marked next day sedation.\[97]

### History
Zopiclone was developed, and first introduced in 1986, by Rhône-Poulenc S.A., now part of Sanofi-Aventis, the main worldwide manufacturer. Initially, it was promoted as an improvement on benzodiazepines, but a recent meta analysis found that zopiclone was no better than benzodiazepines in any of the aspects assessed. On April 4, 2005, the U.S. Drug Enforcement Administration listed zopiclone under Schedule IV, due to evidence that the drug has addictive properties similar to benzodiazepines.

Zopiclone, as traditionally sold worldwide, is a racemic mixture of two stereoisomers, only one of which is active. In 2005, the pharmaceutical company Sepracor of Marlborough, Massachusetts began marketing the active stereoisomer eszopiclone under the name Lunesta in the United States. This had the consequence of placing what is a generic drug in most of the world under patent control in the United States. Although it was expected to be available in generic form by 2010, no generic has become available there at present. However, Zopiclone is currently available off-patent in a number of European countries, as well as Brazil, Canada, and Hong Kong. The eszopiclone/zopiclone difference is in the dosage—the strongest eszopiclone derivative dosage contains 3 mg of the therapeutic stereoisomer, whereas the highest zopiclone dosage (7.5 mg) contains 3.75 mg of the active stereoisomer. The two agents have not yet been studied in head-to-head clinical trials to determine the existence of any potential clinical differences (efficacy, side-effects, developing dependence on the drug, safety, etc.); the significant possibility that the two drugs have identical effects and differ only in dosing, and the simple fact that investing in clinical trials is a very expensive undertaking may be responsible for this line of inquiry thus far remaining unpursued.

Recreational use

Zopiclone is a drug with the potential for misuse and dosage escalation, drug abuse, and drug dependence. Zopiclone is well-known among drug addicts as a drug of abuse, and they commonly seek it from their doctors. [One addiction centre found that 5.1% of drug addicts at their treatment center reported a zopiclone addiction.] It is abused orally and sometimes intravenously and often combined with alcohol to achieve a combined sedative hypnotic—alcohol euphoria. Patients abusing the drug are also at risk of dependence. Withdrawal symptoms can be seen after long-term use of normal doses even after a gradual reduction regime. The Compendium of Pharmaceuticals and Specialties recommends that zopiclone prescriptions not exceed 7 to 10 days, owing to concerns of addiction, drug tolerance, and physical dependence. Two types of drug misuse can occur: either recreational misuse, wherein the drug is taken to achieve a high, or when the drug is continued long-term against medical advice. Zopiclone may be more addictive than benzodiazepines. Those with a history of substance misuse or mental health disorders may be at an increased risk of high dose zopiclone misuse. High dose misuse of zopiclone and increasing popularity amongst drug abusers who have been prescribed with zopiclone The symptoms of zopiclone addiction can include depression, dysphoria, hopelessness, slow thoughts, social isolation, worrying, sexual anhedonia, and nervousness.

Zopiclone and other sedative hypnotic drugs are detected frequently in cases of people suspected of driving under the influence of drugs. Other drugs including the benzodiazepines and zolpidem are also found in high numbers of suspected drugged drivers. Many drivers have blood levels far exceeding the therapeutic dose range and often in combination with other alcohol, illegal, or prescription drugs of abuse, suggesting a high degree of abuse potential for benzodiazepines, zolpidem, and zopiclone. Zopiclone, which at prescribed doses causes moderate impairment the next day, has been estimated to increase the risk of vehicle accidents by 50 percent, causing an increase of 503 excess accidents per million drivers.
accidents per 100,000 persons. It was recommended that zaleplon or other nonimpairing sleep aids be used instead of zopiclone to reduce road traffic accidents.[111] Zopiclone as with other hypnotic drugs is sometimes abused to carry out criminal acts such as sexual assaults.[112]

Zopiclone has cross-tolerance with barbiturates and is able to suppress barbiturate withdrawal signs. Zopiclone is frequently self-administered intravenously in studies on monkeys suggesting a high risk of abuse potential.[113]

Zopiclone is in the top-ten medications obtained using false prescription in France.[43]

However, due to its distinctly bitter taste, it is unlikely to be covertly administered to facilitate drug-related crime such as robbery and sexual assault. The tablets are coated with a film to mask the taste when swallowed, but crushing destroys this film. Also, a common side-effect is a bitter, metallic taste following ingestion, so a person having been administered zopiclone is likely to be aware that they are under the influence of this drug.

Zopiclone enhances the disorientating effects of psychedelic drugs, such as LSD, and would be a bad choice for medical professionals to use to calm down someone suffering a "bad trip".

**Overdose**

Zopiclone is sometimes used as a method of suicide.[114] Zopiclone has a similar fatality index as benzodiazepine drugs, apart from temazepam which is particularly toxic in overdosage.[115][116][117] Deaths have occurred from zopiclone overdose, alone or in combination with other drugs.[118][119][120] Overdose of zopiclone may present with excessive sedation and depressed respiratory function that may progress to coma and possibly death.[121] Zopiclone combined with alcohol, opiates, or other CNS depressants may be even more likely to lead to fatal overdoses. Zopiclone overdose can be treated with the benzodiazepine receptor antagonist flumazenil, which displaces zopiclone from its binding site on the benzodiazepine receptor, thereby rapidly reversing the effects of zopiclone.[122][123] Serious effects on the heart may also occur from a zopiclone overdose[124][125] when combined with piperazine.[126]

Death certificates show the number of zopiclone related deaths is on the rise.[127] Zopiclone when taken alone usually is not fatal, however, when mixed with alcohol or other drugs such as opioids, or in patients with respiratory, or hepatic disorders, the risk of a serious and fatal overdose increases.[128][129]

**Detection in biological fluids**

Zopiclone may be measured in blood, plasma, or urine by chromatographic methods. Plasma zopiclone concentrations are typically less than 100 μg/L during therapeutic usage, but frequently exceed 100 μg/L in automotive vehicle operators arrested for impaired driving ability and may exceed 1000 μg/L in acutely poisoned patients. Postmortem blood concentrations are usually in a range of 0.4-3.9 mg/L in victims of fatal acute overdosage.[130][131][132]

**See also**

- Benzodiazepine
- Benzodiazepine dependence
- Benzodiazepine withdrawal syndrome
- Nonbenzodiazepine
- Pazinaclone
- Zaleplon
- Z drugs

References


41. ^ Professor Heather Ashton. "BENZODIAZEPINES: HOW THEY WORK AND HOW TO WITHDRAW" (http://www.benzo.org.uk/manual/).


50. ^ Kripke, Daniel F (2008). "Evidence That New Hypnotics Cause Cancer" (http://repositories.cdlib.org/cgi/viewcontent.cgi?article=1002&context=ucsdpsych) (PDF). *Department of Psychiatry, UCSD* (University of California). "the likelihood of cancer causation is sufficiently strong now that physicians and patients should be warned that hypnotics possibly place patients at higher risk for cancer."


**External links**

- Detailed pharmacological information (http://www.mentalhealth.com/drug/p30-i01.html)
- Scheduling recommendation (http://www.erowid.org/pharms/zopiclone/zopiclone_law1.pdf) (PDF file)
- Details on scheduling (http://www.deadiversion.usdoj.gov/fed_regs/rules/2005/fr0404.htm)
- Erowid zopiclone vault (http://www.erowid.org/pharms/zopiclone/zopiclone.html)
- Support for Zopiclone dependency/addiction (http://www.non-benzodiazepines.org.uk/)