

Etizolam

(Trade Names: Etilaam, Etizest, Depas, Etizola, Sedekopan, Pasaden)

Introduction:

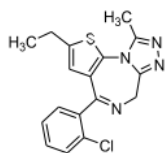
Etizolam is a thienodiazepine which is chemically related to a class of substances known as benzodiazepines. Benzodiazepines produce central nervous system (CNS) depression and are commonly used to treat insomnia and anxiety. Etizolam is currently a prescription medication in Japan, India and Italy but has recently emerged on the illicit drug market in Europe and the United States. Etizolam is usually encountered in powder form or in tablet form. Etizolam has also been encountered spiked onto blotter paper.

Licit Uses:

Benzodiazepines are widely prescribed drugs; however, etizolam is not approved for medical use in the United States. Additionally, etizolam is used as a prescription medication in some countries. Etizolam was introduced in 1983 in Japan as a treatment for neurological conditions such as anxiety and sleep disorders. It is currently available as 0.25 mg, 0.5 mg and 1.0 mg tablets in countries where it is marketed for clinical use.

Chemistry:

Etizolam (4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine) has a similar structure to the benzodiazepine class of compounds. Etizolam has a thiophene ring, in place of a benzene ring found in the benzodiazepine class, fused to a seven-membered 1,4diazepine ring. Etizolam also contains a fused triazolo ring. A 2-chlorophenyl ring is attached at the 4-position and an ethyl group is attached at the 2-position of the thienodiazepine ring structure. Etizolam has a molecular formula of C₁₇H₁₅ClN₄S and a molecular weight of 342.8 g/mol. The structure of etizolam is shown below:



Pharmacology:

Etizolam, a thienodiazepine derivative, was approved for the management of anxiety disorders associated with depression, panic disorder and insomnia in some countries. Pharmacologically, etizolam is a benzodiazepine and possesses CNS depressant effects, such as anxiolytic, anticonvulsant, sedative-hypnotic and muscle relaxant effects. Unlike diazepam (Valium®), it has some imipramine-like neuropharmacological and behavioral effects in preclinical studies. In animal experiments, etizolam is 6-10 times more potent than diazepam in most of its pharmacological effects. Etizolam has been demonstrated to have some reinforcing effects in monkeys. In physical-dependence studies in animals, it substituted for barbitals and produced withdrawal signs typical of the sedative-hypnotic class. Drug discrimination studies in monkeys indicated that it had pentobarbital-like effects. Clinical studies suggest that etizolam is approximately 10 times as potent as diazepam in producing hypnotic effects. In a single-dose pharmacokinetic study in humans, etizolam was rapidly absorbed with the maximum plasma concentration occurring within 0.5-2 hours and the mean elimination half-life averaged 3.4 hours. Clinical observations of physical dependence on etizolam were also reported. Major adverse effects include drowsiness, sedation, muscle weakness and incoordination, fainting, headache, confusion, depression, slurred speech, visual disturbances and changes in libido and tremor.

Illicit Uses:

Despite the relative age of etizolam, in recent years there has been a rise in its abuse, which has led to its classification as a novel psychoactive substance benzodiazepine. Recently, etizolam has been named an emerging substance of abuse and has been increasingly identified in toxicology samples, as an adulterant in seized samples, and has been involved in increased numbers of reported driving under the influence of drugs (DUID) cases. In September 2014, the Blue Ridge Poison Center called etizolam an emerging drug of concern.

Additionally they stated there has been an upward trend in Poison Control Center calls. The United Nations Office on Drugs and Crime (UNODC) Toxicology Portal reports for 2019 and 2020 indicate that etizolam is being used in a number of countries in Europe including but not limited to Switzerland, Sweden, Canada, and Australia. According to the United Nations Office on Drugs and Crime (UNODC Current NPS Threats, 2022), benzodiazepine-type novel psychoactive substances (NPS) continue to constitute the greatest number of NPS reported to the Tox-Portal, accounting for 47% of all NPS cases associated with postmortem investigations, and 67% of all DUID cases. Of the substances reported, etizolam was the most common, accounting for 141 reported cases. The Centers for Disease Control and Prevention recently released "The Fentalog Study", which utilizes data collected from 10 geographically diverse hospitals in 9 states across the United States. As of March 2023, out of 733 samples tested between February, 2020 and December 2022, 9% of blood specimens from suspected opioid-involved overdoses also tested positive for illicit benzodiazepines. Etizolam was positively identified in twenty-two percent of these illicit benzodiazepine, opioid-involved overdoses.

User Population:

Although it is a legitimate pharmaceutical product in Japan, Italy and India, etizolam is used as a recreational substance in the United States. Information suggests that a broad range of populations including youths, young adults and older adults, use etizolam. The population likely to abuse etizolam appears to be the same as those abusing prescription benzodiazepines, barbiturates, and other sedative hypnotic substances. This is evidenced by drug user reports associated with these substances.

Illicit Distribution:

Etizolam is purchased via the internet and at local retail shops where it is promoted as a "research chemical." It has been sold as a powder, in tablet form and spiked onto blotter paper. The DEA's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. According to NFLIS-Drug, there were 1,722 reports of etizolam submitted to NFLIS-Drug in 2018, 3,751 in 2019, 5,231 in 2020, 4,325 in 2021, and 1,170 in 2022.

Control Status:

Etizolam is currently controlled under Schedule I of the Controlled Substances Act. At the 2020 Commission on Narcotic Drugs Sixty-third session, the Commission decided to include etizolam in Schedule IV of the 1971 Convention on Psychotropic Substance.