

ETIZOLAM

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

Introduction:

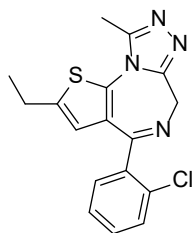
Etizolam is a thienodiazepine, which is chemically related to a class of substances known as benzodiazepines. Benzodiazepines produce central nervous system (CNS) depression and are commonly used to treat panic disorders, insomnia, and anxiety. Etizolam is currently a prescription medication in Japan, India, and Italy, but this substance 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. In some other countries, etizolam is used as a prescription medication. In Japan, etizolam was introduced in 1983 as a treatment for neurological conditions, such as anxiety and sleep disorders. In countries that market etizolam for clinical use, this substance is available as 0.25 mg, 0.5 mg, and 1.0 mg tablets.

Chemistry:

Etizolam is chemically known as 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine. Etizolam has a similar structure to the benzodiazepine class of compounds; however, the benzene ring found in benzodiazepines is replaced by a thiophene ring fused to a seven-membered 1,4-diazepine 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 $C_{17}H_{15}ClN_4S$ 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®), etizolam 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. In monkeys, etizolam has been demonstrated to have some reinforcing effects. In physical-dependence studies in animals, etizolam substituted for barbitol and produced withdrawal signs typical of the sedative-hypnotic class. Drug discrimination studies in monkeys indicated that etizolam had pentobarbital-like effects. Clinical studies suggest that etizolam is approximately 10 times more potent than 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:

Etizolam has been increasingly abused in recent years and therefore classified as an emerging substance of abuse and novel psychoactive substance (NPS) benzodiazepine. Etizolam has been increasingly detected in toxicology samples, identified as an adulterant in seized samples, and involved in greater numbers of reported driving under the influence of drugs (DUID) cases.

In September 2014, the Blue Ridge Poison Center reported an upward trend in Poison Control Center calls and named etizolam an emerging drug of concern. Since 2019, the United Nations Office on Drugs and Crime (UNODC) Early Warning Advisory on NPS Toxicology Portal (Tox-Portal)—an online tool to collect toxicological and harm data associated with NPS use—has published biannual reports (Current NPS Threats) to identify most harmful NPS. These reports indicate that etizolam is used in European countries, such as Switzerland and Sweden, as well as Canada and Australia. In 2023, etizolam was the most common benzodiazepine-type NPS reported in postmortem (n=30) and DUID (n=45) cases and was also reported in drug-facilitated crime cases. In 2024, UNODC reported that benzodiazepine-type NPS continued to constitute the greatest number of NPS reported to the Tox-Portal across postmortem, DUID (68%), and clinical admission (56%) cases. More recently, the Centers for Disease Control and Prevention released “The Fentalog Study”, which utilizes data collected from 10 geographically diverse hospitals in 9 states across the United States. As of December 2024, the study tested 1,476 samples between February 2020 and August 2024; of these, 8% of blood specimens from suspected opioid-involved overdoses tested positive for illicit benzodiazepines and etizolam was positively identified in 15% of these specimens.

User Population:

Although etizolam 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 can be purchased via the internet and at local retail shops where the substance is promoted as a “research chemical.” Etizolam has been sold as a powder, in tablet form, and spiked onto blotter paper.

The Drug Enforcement Administration’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. NFLIS-Drug received 1,722 reports of etizolam in 2018; 3,752 in 2019; 5,259 in 2020; 4,443 in 2021; 1,478 in 2022; 425 in 2023; and 150 in 2024 (reports still pending).

Control Status:

Etizolam is controlled in schedule I of the Controlled Substances Act. At the 2020 Commission on Narcotic Drugs’ 63rd session, the Commission decided to include etizolam in Schedule IV of the 1971 Convention on Psychotropic Substances.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.