

Etizolam

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

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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.

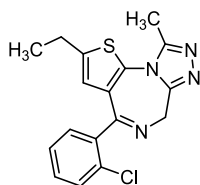
Etizolam is usually encountered in powder form or in tablet form. Etizolam has also been encountered spiked onto blotter paper.

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-6Hthieno[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 $C_{17}H_{15}ClN_4S$ 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®), 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 barbitol 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:

In recent years there has been a rise in the abuse of etizolam. 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.

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.

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 National Forensic Laboratory Information System (NFLIS) is a DEA database that collects scientifically verified data on drug items and cases submitted to and analyzed by state, local, and federal forensic laboratories. The System to Retrieve Information from Drug Evidence (STRIDE)/STARLiMS provides information on drug seizures reported to and analyzed by DEA laboratories. According to NFLIS, the number of etizolam drug reports have steadily increased from 3 in 2012, to 600 reports in 2016, 950, in 2017, and 1,570 in 2018. In the first nine months of 2019, there were 953 drug reports of etizolam submitted within the NFLIS database, in which roughly 4,870 reports were from 46 states from 2012 through September of 2019. There were no reports of etizolam in NFLIS and/or STRIDE/STARLiMS prior to 2012.

Control Status:

Etizolam is not currently controlled under the Controlled Substances Act.

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