

## 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 are a class of drugs that 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.

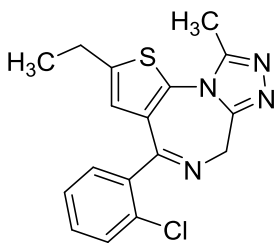
Etizolam is usually encountered in powder form or in tablet form. Etizolam has also been encountered spiked onto blotter paper.

### Licit Uses

Benzodiazepines are widely prescribed drugs; however, etizolam does not currently have an accepted medical use in the United States. 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 1,4-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<sup>®</sup>), 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.

### 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 etizolam is used by a broad range of population groups including youths, young adults and older adults.

### Illicit Distribution

Etizolam is sold over 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 and local forensic laboratories. The System to Retrieve Information from Drug Evidence (STRIDE) provides information on drug seizures reported to and analyzed by DEA laboratories. According to NFLIS and STRIDE, the number of etizolam drug reports increased from 3 in 2012 to 92 in 2013. In the first six months of 2014, there were 45 reports of etizolam in the NFLIS and STRIDE databases. There were a total of 140 drug reports of etizolam from 21 states from 2012 through June of 2014. There are no reports of etizolam in NFLIS or STRIDE prior to 2012.

### Control Status

Etizolam is not currently listed under the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 202-353-1263, telephone 202-307-7183, and Email ODE@usdoj.gov.