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Drug overview: Etizolam is a benzodiazepine analogue, a thienodiazepene.¹ It has gathered some popularity on the new psychoactive substance (NPS) market in the UK and Europe.

Chemical name(s): 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4] diazepine.²

Brand Names: Etilaam, Etizest, Etizola, Sedekopan,

Depas, Pasaden.³

Classification: Depressant.

Background: Etizolam is unlicensed in the UK although used as a prescribed medication in other countries such as India, Italy and Japan.^{4,5,6} A 1mg tablet is equivalent to a 10mg diazepam (Valium) tablet.⁷

Appearance: Etizolam typically comes in 1mg and 2mg tablets which are often described by online vendors as 'pellets'. Its appearance can vary depending on the source of purchase: tablets can be blue, pink or white and more increasingly may be sold as 'street Valium' and therefore can appear as light blue tablets with commonly-seen Valium markings. When sold as etizolam, it can be found in a foil strip packet with the brand name on the foil

such as Etilaam or Etizest. There are other tablets in circulation which are lighter blue (similar to blue diazepam colour) and can display the markings EZ. Tablets from other vendors may simply come as unmarked blue, pink or white pills that come loose in a zip-seal plastic bag.⁸

It is also possible to purchase in powder form, which is often white.¹⁰ Anecdotal reports suggest that it is rare for users to purchase the powder form in the UK.

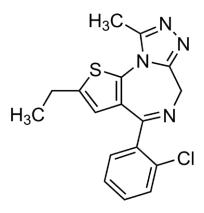


Image: Wikimedia commons



Image: Police Scotland 9







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Cost: Etizolam varies in cost, depending on the form and quantity purchased. They can range from £1 for single tablets (or in quantities less than 10), to as low as 5p per tablet at larger quantities. 100 tablets typically cost around £40. The powder form ranges from approximately £10 for 50mg, to £950 for 20 grams.¹¹

Route of administration: Etizolam is generally consumed orally, by swallowing tablets or powder placed into gel capsules.⁸ It can also be taken sublingually (under the tongue).¹⁰ There are reports of snorting and rectal administration although this appears to be rare on the UK scene.

Legal Status: Etizolam was classified as a Class C drug in the May 2017 amendment to The Misuse of Drugs Act 1971.²³

Dosage (when prescribed):12

| Anxiety disorder | 0.25-0.5mg twice daily | |
|----------------------|------------------------|--|
| Panic disorder | 0.5mg twice daily | |
| Insomnia | 1-2mg daily | |
| Maximum daily dosage | 3mg | |

Current guidance for prescribing benzodiazepines is that they should not be prescribed beyond two weeks to prevent dependence.²⁷ A gradual taper strategy when stopping etizolam is also recommended to ease any withdrawal effects. There is limited data on etizolam toxicity in the literature.

Recreational oral dose:8

| Light | Common | Strong | Heavy |
|-------|--------|--------|-------|
| 0.5mg | 1-2mg | 3-4mg | 5mg+ |

Onset, duration and after effects: Oral doses have an onset of 30-60 minutes and peak at 3-4 hours. The duration is generally 6-8 hours although higher doses can last longer. Usual after effects are between 1-5 hours although many users report little after effects, especially if they have had a 7-8 hour period of uninterrupted sleep after use.¹³

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In therapeutic doses, the plasma elimination half-life is between 3.4 and 6 hours (normal daily dosage is up to 2mg/day in divided doses, as per the manufacturer).^{1,12}

However, etizolam has an active main metabolite, alpha-hydroxyetizolam, with an elimination half-life of about 8.2 hours.¹

Typical effects and side effects:These are some of the typical effects and side effects experienced by people who use etizolam. Not everyone will experience all of the effects listed and many can be dosedependent. Overall, etizolam is reported to be "well tolerated with little side effects" when prescribed.

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Physical effects

Decrease in energy, decreased heart rate, impaired coordination, sleepiness, respiratory depression, blurred vision, yawning, constricted pupils, decreased appetite, nausea and vomiting, muscle relaxation, dry mouth, headache, involuntary eye closure, rebound insomnia (prolonged use).

Mental effects

Mood enhancement, relaxation, reduced anxiety, lowered inhibitions, sedative effects, mental confusion, short term memory loss

Comedown effects: Some users report malaise after use but the majority of people who use on an occasional basis suggest there is little comedown or hangover. Using on a more frequent basis can lead to rebound anxiety and/or depression, with difficulty sleeping, problems falling asleep or waking early.

Brain chemistry and pharmacological effects: Etizolam is a full benzodiazepine receptor agonist and so has a broadly similar pharmacological profile to benzodiazepine drugs such as diazepam.¹⁵ It has the full range of group-specific benzodiazepine effects: anxiolytic, sedative, hypnotic, anticonvulsant and muscle relaxant, and is approximately 10 times more potent than diazepam.⁷ It differs from drugs such as diazepam as it has selective and high affinity binding to postsynaptic GABA-A receptor alpha₂ subunit, which results in specific anxiolytic effects.¹⁶

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Patterns of use: Patterns of use appear to be similar to other benzodiazepines. Some users report using etizolam as a comedown aid after using stimulant or psychedelic drugs.

Etizolam has been a growing feature in drug related deaths. It is not clear from the statistics whether people have intended to take etizolam or have believed it to be street Valium. In Scotland in 2016, there were 286 deaths for which NPSs were implicated in, or potentially contributed to the cause of death. In 277 cases, the only NPSs present were benzodiazepines (usually etizolam, but sometimes other unlicensed benzodiazepines such as diclazepam or phenazepam).²⁸

Tolerance, dependence and withdrawal: Benzodiazepines such as etizolam which are more rapidly eliminated from the body are less likely to accumulate, ¹⁷ and there

is evidence to suggest that etizolam is less likely to induce tolerance and dependence compared with classical benzodiazepines.¹⁸

However, dependence may develop with regular use of benzodiazepines, even in therapeutic doses for short periods. If benzodiazepines are discontinued abruptly after regular use, withdrawal symptoms may develop. Administration of regular doses of benzodiazepines can result in physical dependence,



Image: Wikimedia commons

characterized by a withdrawal syndrome when the drug is discontinued. With larger doses, the physical dependence develops more rapidly.¹⁹

Withdrawal symptoms include: anxiety, insomnia, headache, dizziness, tinnitus, anorexia, vomiting, nausea, tremor, weakness, perspiration, irritability, hypersensitivity to visual and auditory stimuli, palpitations, tachycardia (fast heart rate) and postural hypotension (drop in blood pressure on standing). In severe and rare cases of withdrawal from high doses, patients may develop affective disorders or motor dysfunction: seizures, psychosis, agitation, confusion, and hallucinations.^{20,21}

There is also evidence that links benzodiazepine use (in conjunction with alcohol) as a factor in offending.²²





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Long term effects/known harms: Etizolam is entirely metabolised by the liver and so is contraindicated in those with liver function issues.²⁵ Loss of hypnotic effects and increased tolerance may be experienced with long term use. There is also a risk of dependence and addiction with repeated use.

Benzodiazepines commonly cause drowsiness, ataxia (neurological conditions which affect balance and coordination), dysarthria (difficulty speaking), nystagmus (involuntary eye movement) and blepharospasm (involuntary closure of eyelids). Coma, hypotension (low blood pressure), bradycardia (slow heart beat) and respiratory depression occasionally occur but are seldom serious if these drugs are taken alone. Coma usually lasts only a few hours but may be prolonged in elderly patients.

Benzodiazepine respiratory depressant effects are more serious in patients with severe chronic obstructive airways disease. Severe effects in overdose also include rhabdomyolysis (breakdown of muscle tissue) and hypothermia.

Co-ingestion of alcohol and other central nervous system depressants potentiates the effects of benzodiazepines and can increase toxicity.

Harm reduction advice for clients, if determined to use:

- Try a small test amount (e.g. 0.5mg) and wait at least 1 hour before taking any more.
- Avoid mixing with alcohol. 12
- Etizolam can increase the risk of drowsiness, ataxia (problems with movement, balance and speech) and disturbances of consciousness if taken with neuroleptics, antidepressants, antihistamines, analgesics, antiepileptics or other similar prescribed medications.¹²
- Control quantities taken in one session.
- Try not to use alone and tell friends what they are taking.
- Place sleeping people in the recovery position. If going to sleep, sleep on their side.
- Do not drive or operate machinery.
- Be aware that tolerance and dependency can develop quickly.
- Avoid if they have any history of benzodiazepine addiction.
- Seek help from medical support quickly if they experience any negative side effects.

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Overdose & Emergencies: As unconsciousness or overdose is possible try to make sure a friend is around who is not using the drug. If a user becomes unconscious call an ambulance, then place them in the recovery position to prevent choking (see images below). The recovery position is for someone who is unconscious but breathing normally. If they are not breathing normally CPR is required, with an emphasis on giving supplementary oxygen via rescue breaths.



Start by placing their arm as if they are waving.



Place the other arm across their chest and hold their hand against their cheek.



Lift up the knee that is furthest from you. Continue to hold their hand in place.



Turn them on their side by pulling the knee towards you and down.

For further information on Overdose & Emergencies see UK and Ireland DrugWatch Information Sheet.²⁶

Where to get help: We would advise anyone experiencing issues from etizolam or other substances to seek medical support via their GP or NHS 24 on 08454 24 24 (Scotland) or NHS Direct 111 (England and Wales).

There are a wide range of local drug services throughout the UK, to find out what is available in your area please use the links below:

Scotland: <u>Scottish Drug Services</u> <u>England: Find Support | Frank</u> Wales: Dan 24/7 Northern Ireland: Public Health Agency ROI: Drugs.IE

For further advice, medical professionals can use the National Poisons Information Service 24-hour telephone service on 0344 892 0111 or its online database, TOXBASE. Any health professional encountering an unusual or unexpected adverse reaction to the use of etizolam (or any other drug) should report the reaction to RIDR.





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If you require more information on this briefing or information about NPS training please contact staff at SDF on 0141 221 1175 or you can visit the website: www.sdf.org.uk.

Disclaimer: This information has been collated from a variety of sources including expert users from UK and Europe, information obtained from users through interviews, surveys and questionnaires and information from users via relevant websites and drug forums. This information sheet is to be used as a rough guide only and SDF/Drugwatch cannot vouch that all information is factual as there is little scientific or medical evidence available on the substance and much of the information has been obtained from service users' reports.

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