Drug overview: Etizolam is a benzodiazepine analogue, a thienodiazepene. 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.

Brand Names: Etlaam, Etizest, Etizola, Sedekopan, Depas, Pasadena.

Classification: Depressant.

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

Appearance: Etizolam typically comes in 1mg and 2mg tablets which are often described as ‘pellets’. Its appearance can vary depending on the source of purchase. A popular brand name Etlaam sold online is found in a foil strip packet with 1mg dark blue ‘sugar pill’-sized coated tablets. There are other tablets in circulation which are lighter blue (similar to blue diazepam colour) and can display the markings EZ. The 2mg are often small dark pink coated tablets. Tablets from other vendors may simply come loose in a zip-seal plastic bag.

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

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

Dosage (when prescribed):

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

Similar to benzodiazepines, prescribing guidance is that etizolam should not be prescribed beyond 12 weeks. 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:

<table>
<thead>
<tr>
<th>Light</th>
<th>Common</th>
<th>Strong</th>
<th>Heavy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5mg</td>
<td>1-2mg</td>
<td>3-4mg</td>
<td>5mg+</td>
</tr>
</tbody>
</table>

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.

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). However, etizolam has an active main metabolite, alpha-hydroxyetizolam, with an elimination half-life of about 8.2 hours.
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 dose-dependent. Overall, etizolam is reported to be “well tolerated with little side effects” when prescribed.14.

<table>
<thead>
<tr>
<th>Physical</th>
<th>Mental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in energy</td>
<td>Mood enhancement</td>
</tr>
<tr>
<td>Decreased heart rate</td>
<td>Relaxation</td>
</tr>
<tr>
<td>Impaired coordination</td>
<td>Reduced anxiety</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>Lowered inhibitions</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Sedative effects</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>Mental confusion</td>
</tr>
<tr>
<td>Yawning</td>
<td>Short term memory loss</td>
</tr>
<tr>
<td>Constricted pupils</td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td></td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td></td>
</tr>
<tr>
<td>Muscle relaxation</td>
<td></td>
</tr>
<tr>
<td>Dry mouth</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Involuntary eye closure</td>
<td></td>
</tr>
<tr>
<td>Rebound insomnia (prolonged use)</td>
<td></td>
</tr>
</tbody>
</table>

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 agonist15 and so has a broadly similar pharmacological profile to benzodiazepine drugs such as diazepam. 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 diazepam7. It differs from drugs such as diazepam as it has selective and high affinity binding to postsynaptic GABA-A receptor alpha_2 subunit, which results in specific anxiolytic effects16.

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.
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, 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\(^{22}\).

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.
**Legal Status:** Etizolam is currently not controlled under the Misuse of Drugs Act\(^2^3\).

From 15\(^{th}\) November 2011, new psychoactive substances that cause concern can be made subject to a Temporary Class Drug Order\(^2^4\). Temporary Class Drug Orders can be made by the Home Secretary if a drug is not classified under the Misuse of Drugs Act 1971. Orders can be made if the Advisory Council for the Misuse of Drugs (ACMD) have been consulted and decided an order should be made, or if they have advised the Home Secretary that an order should be made. A TCDO may apply to etizolam in the future.

**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\(^1^2\).
- 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\(^1^2\).
- 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.

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

If you require more information on this briefing or information about legal high training please contact staff at SDF on 0141 221 1175 or you can visit the website www.sdf.org.uk. If you require support regarding a drug issue you can access information about support in your area at www.scottishdrugservices.com (Scotland) or www.drugscope.org.uk/resources/helpfinder (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.

Overdose & Emergencies: See DrugWatch Overdose and Emergencies Information Sheet for further information. 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).

References:

11. Various online suppliers (2014). References not published due to risks of promoting individual web sites.