Etizolam (Depas, Etilaam, Etizest)

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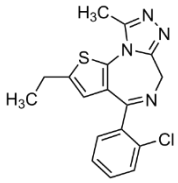
Manufacturer: Mitsubishi Pharma Corporation



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

Mol. Formula: $C_{17}H_{15}ClN_4S$ **Molecular weight:** 342.85

CAS#: 0040054-69-1

Approval: Not approved in the U.S. Approved in Japan, Italy and Korea. Since 1984, the most commonly used anxiolytic in Japan.[1]

Dosage: 0.25-0.50 mg 2-3X/day for anxiety and 1-2 mg before bedtime for insomnia.[2]

Mechanism of action: GABA agonist, which may have selectivity for the subpopulation associated with anxiety.[3]

Pharmakokinetics: In clinical studies, a single 2 mg dose resulted in plasma concentration of 25 ng/mL. Patients dosed 1 mg twice daily had the same concentration.[4]

$T_{1/2}$: 7-15 h[5]; **T_{max}** ~ 3.2 h

Pharmacodynamincs: Anti-anxiety, strong muscle relaxant.[1]

Metabolism: Main metabolites are α-hydroxyetizolam and 8-hydroxyetizolam, both having a longer half-life than parent.[4] Cyp3A4 is the main cytochrome responsible for metabolism with Cyp2C18 and 2C19 playing a minor role. Mutations of Cyp2C19 can cause loss of metabolic activity of that enzyme resulting in a longer $T_{1/2}$ and pharmacological effect. Inducer of Cyp3A4, carbamazepine, significantly decreases C_{max} and T_{max} in healthy volunteers.[2]

Driving and cognitive effect/toxicity: One study on patients using 0.5 mg BID. No deleterious effects were found.[3] Toxic effects include confusion disorientation, ataxia, slurred speech, and delirium.[5]

Toxicology analysis: Etizolam and its two main metabolites have been characterized from whole blood by GC-MSMS following SPE clean-up.[4] Our laboratory has detected the drug from a case by GCMS following a standard SB LLE extraction (Fig. 1, RRT = 2.42, mepivacaine I.S., elutes after alprazolam and before trazodone, DB-5 column: 30 m X 0.25 mm (i.d.), 0.25 um).

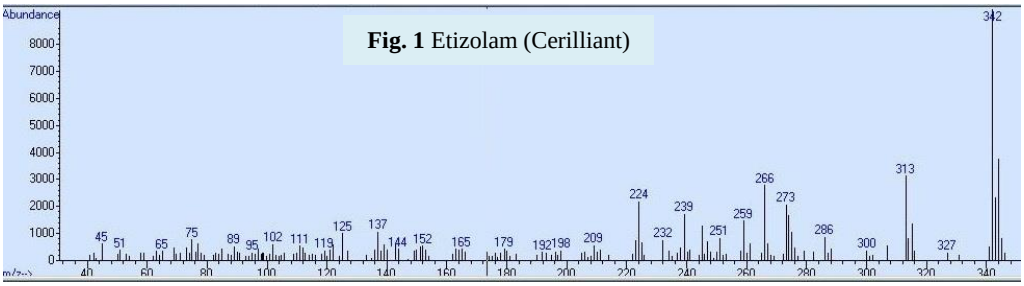


Fig. 1 Etizolam (Cerilliant)

References:

1. PDF (search for etiolam) in http://www.mt-pharma.co.jp/e/
2. Mandrioli, R., *et. al.* Current Drug Metabolism 2008, 9, 827-844.
3. De Candia, M.D., *et. al.* Clinical Therapeutics, 2009, 31, 2851.
4. Nakamae, T., *et. al*. Forensic Science International, 2008, e1-e6.
5. Baselt. Disposition of Toxic Drugs and Chemicals in Man. 8th Ed.