Etizolam (Depas, Etilaam, Etizest)

Stephanie Hopkins, stephanie.hopkins@doj.ca.gov California Department of Justice, 4949 Broadway, Room F-249, Sacramento CA, 95820.

Manufacturer: Mitsubishi Pharma Corporation

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

Mol. Formula: C_{17}H_{15}ClN_{4}S 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 h⁵; T_{max} ~ 3.2 h

Pharmacodynamics: 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.⁷ 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/
5. Baselt. Disposition of Toxic Drugs and Chemicals in Man. 8th Ed.