

Drug Status Report

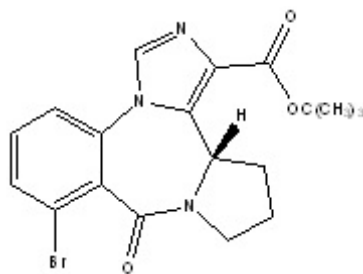
Drug: Bretazenil

Drug Name Status: Bretazenil is the proper name (INN).

Chemical Name: tert-Butyl (S)-8-bromo-11,12,13,13 α -tetra-hydro-9-oxo-9H-imidazo[1,5- α]pyrrolo[2,1-c][1,4-benzodiazepine-1-carboxylate

Other names: 9H-Imidazo(1,5- α)pyrrolo(2,1-c)(1,4)benzodiazepine-1-carboxylic acid, 8 bromo-11,12,13,13 α -tetrahydro-9-oxo, 1,1-dimethylethyl ester, (S)-; Ro 16-6028

Chemical structure:



Molecular Formula: C₁₉H₂₀BrN₃O₃

Pharmacological class / Application: benzodiazepine receptor partial agonist

International status:

US: Bretazenil is not listed on any of the Schedules to the CSA and is not mentioned on the DEA website.

United Nations: Bretazenil is not listed on the Yellow List - List of Narcotic Drugs under International Control nor the Green List - List of Psychotropic Substances under International Control.

Canadian Status: Bretazenil is a tetracyclic imidazodiazepine drug that is used to treat anxiety. *In vivo* studies have shown that bretazenil acts as a partial agonist at the benzodiazepine receptor and is associated with a lower abuse potential compared to classical benzodiazepines¹. While bretazenil is often referred to as a benzodiazepine derivative, the substance is not derived from any of the substances listed under Item 18 of Schedule IV to the CDSA, but rather is synthesized via the pyrrolobenzodiazepine, (S)-6-bromo-1,2,3,11 α -tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-

¹Busto, U. *et al.* (1994) Pharmacologic effects and abuse liability of bretazenil, diazepam, and alprazolam in humans, *Clin. Pharmacol. Ther.* **55**:451-463

5,11(10H)-dione, from 6-bromoisatoic acid anhydride and L-proline as starting materials^{2,3}. In addition, bretazenil does not contain the core structure of the benzodiazepines listed in Item 18 of Schedule IV to the CDSA.

Therefore, while bretazenil acts as a partial agonist at the benzodiazepine receptor it should not be included in Item 18 of Schedule IV to the CDSA since the substance does not contain the essential benzodiazepine structure.

Recommendation: Bretazenil is not included in item 18 of Schedule IV to the CDSA and is not a controlled substance.

April 7th 2010.

²Hunkeler, W. *et al.* (1982) Diazepine derivatives, US Patent 4,353,827.

³Katsifis, A. *et al.* (1996) Synthesis of iodine-123 labelled analogues of the partial agonist (S)- and (R)-bretazenil for the study of CNS benzodiazepine receptors using SPECT, *J. Labelled Compounds and Radiopharm.* **38**:835-845.