California Association of Toxicologists

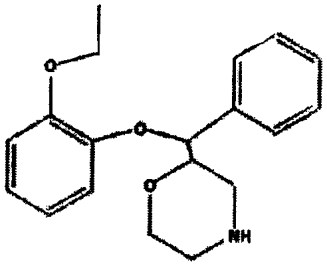
New Drugs Committee Report

Reboxetine (Vestra®)

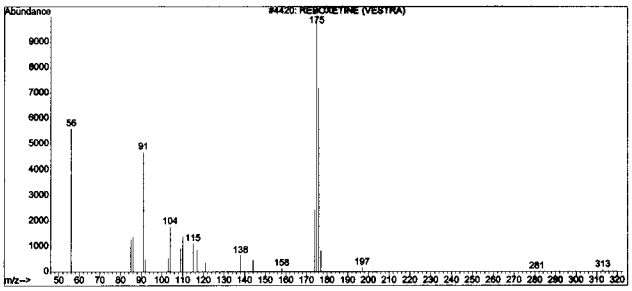
General

Reboxetine is a *very* new anti-depressant manufactured by Pharmacia & Upjohn and is currently distributed in Europe under the trade name Edronax®. The drug is considered a selective norephinephrine reuptake inhibitor (SNRI) that works on the norephinephrine chemical pathway in the brain. Reboxetine received FDA approval in July 1999 and is being dispensed as reboxetine mesylate tablets.

Chemical



- Reboxetine methansulfonate
  - (2RS,3RS)-2-(alpha-(2-Ethoxyphenoxy)benzyl)morpholine methanesulfonate
  - $C_{19}H_{23}NO_3$-CH_4SO_3
  - Formula weight 409.51
  - Molecular weight 313.39
- White powder soluble in methanol and dimethylformamide. Partially soluble in ethanol and water.
- Reboxetine is a basic drug and can be extracted with an n-butylchloride liquid/liquid extraction and an acid back extraction.
- Detection of reboxetine is possible on either a GC/NPD or GC/MS.



Ions: 175, 176, 91, 56, 174, & 313 m/z

Relative retention time of Reboxetine (1.304/Carbinoxamine) to other commonly encountered basic drugs are as follows:
Promethazine, Bupivicaine, Benztropine, **REBOXETINE**, Norsertraline, Sertraline, Codiene

Pharmacology

- Reboxetine is metabolized in the liver to O-Desmethylreboxetine, its primary metabolite, and three minor metabolites.
- Absorbs rapidly, T_{max} ~ 2 hours
- Half-life: 13 hours
- Bioavailability: 92 %
- Urinary Excretion: 9% of dose
- Clinical Trials

Dose	C_{max}	
1.5 mg	38.3 $\pm$ 13.5	ng/ml
3.0 mg	76.6 $\pm$ 26.3	ng/ml
4.5 mg	99.8 $\pm$ 24.1	ng/ml
5.0 mg	164	ng/ml