

New Drugs

DULOXETINE (Cymbalta®)

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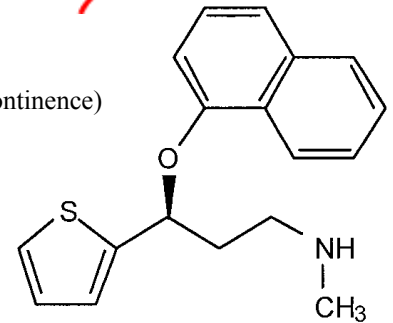
Duloxetine (Cymbalta®), manufactured by Eli Lilly and Company, was first approved in the US by the FDA on August 3, 2004 for the treatment of major depressive disorder. The drug is a potent reuptake inhibitor of serotonin and norepinephrine. In addition, the FDA approved duloxetine, in September 2004, for the management of pain associated with diabetic peripheral neuropathy.

General Information

Common Name:	Duloxetine HCL
Trade Names:	Cymbalta®, Yentreve® (Europe-Female urinary incontinence)
Chemical Name:	2-Thiophenepropanamine, N-methyl-gamma-(1-naphthalenyloxy)-,hydrochloride,(gammaS)-
Chemical Formula:	C ₁₈ H ₁₉ NOS · HCl
Formula Weight:	333.88
Molecular Weight:	297
CAS Number:	136434-34-9
Capsule Size:	20, 30 & 60 mg strengths (delayed release)
Dosage:	Dose 40-60 mg/day (given as 20 or 30 mg BID) for depression Dose 60 mg/day given once a day for diabetic peripheral neuropathic pain



Lilly



Pharmacology

Half-Life:	~12 hours (8-17 hours)
Absorption:	C _{max} occurs within 6-10 hours of oral dose
Elimination:	Primarily through hepatic metabolism – P450 (CYP2D6 & CYP1A2) Desmethyl duloxetine (active) and Hydroxy metabolite (active)
V _d :	1640 L
Oral Doses:	Given oral doses 20 mg, mean peak plasma level of 13 ng/ml
Mechanism of Action:	Dual-selective serotonin and norepinephrine reuptake inhibitor. Structurally unrelated to venlafaxine and milnacipran, the mechanism and pharmacodynamic characteristics are similar. Structurally similar to fluoxetine and atomoxetine.

Toxicology

Extraction:	Extracts as a basic drug utilizing an n-butylchloride liquid/liquid basic drug extraction; survives an acid back extraction.
Detection:	Although one would think that it should behave similar to other Anti-depressant drugs, this particular one does not respond very well on a GC/NPD. Response on GC/MS is good. Linearity and detection limits are yet to be determined.
Elution Order:	Norsertaline, Sertraline, Citalopram, DULOXETINE , Diazepam, Paroxetine

