

NEW DRUG - Pregabalin (Lyrica®)



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The Food and Drug Administration approved Pregabalin in December 2004 for the treatment of nerve pain associated with diabetes and shingles. Pregabalin, developed by Pfizer, has a novel mechanism of action that works by reducing the number of signals that are sent out from the damaged nerves. This provides fast and sustained relief from neuropathic pain often characterized by a “pins and needles” feeling. Pregabalin has also been approved for the relief of partial onset seizures in adults with epilepsy. It is prescribed in capsules of 25, 50, 75, 100, 150, 200, 225, and 300 mg doses.



Pharmacokinetics

Pregabalin is readily absorbed orally, and its oral bioavailability is equal to or greater than 90%. It has a half-life of about 6 hours. Pregabalin reaches a peak plasma concentration (means range from 0.04 to 9.5 ug/mL) within 1.5 hours. Following single-dose (25-300 mg) and multiple-dose (75-900 mg/day) administration, maximum plasma concentrations increase linearly, with steady-state levels reached within 24 to 48 hours. Patients taking the recommended dosages have shown steady state concentrations up to 10 ug/mL. Pregabalin has a volume of distribution of 0.5 L/kg. Approximately 90% of the dose is excreted unchanged in the urine. The N-methylated derivative of pregabalin is the major urinary metabolite, accounting for only 0.9% of the dose.

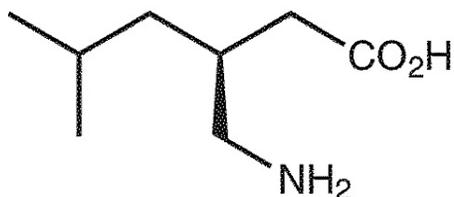
Chemistry

Pregabalin has a molecular weight of 159.23 (C₈H₁₇NO₂). It has two pK_a values, 4.2 and 10.6, corresponding to the carboxylic acid and the amine groups, respectively. It is freely soluble in water and both basic and acidic aqueous solutions. A reference standard, provided by Pfizer Global Research & Development, was dissolved in methanol to create a working standard of 1 mg/ml.

Pregabalin was analyzed by protein precipitation of samples with acetonitrile and detection by LC/MS/MS. Multiple Reaction Monitoring (MRM) mode was utilized with one transition for qualification and one for quantification. Separation was achieved on a C-18 column using a gradient elution with methanol and water. Calibrators in the concentration range of 1.0 to 25 ug/mL were used for quantitation. The Los Angeles County Department of Coroner Toxicology Laboratory has analyzed casework with postmortem blood levels ranging from 2.7 to 22 ug/mL.

IUPAC name:

(S)-3-(aminomethyl)-5-methylhexanoic acid



Reference: Thomson Micromedex® Healthcare Series, 2007

