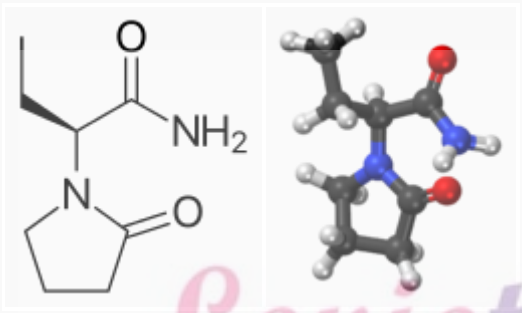
Levetiracetam

Levetiracetam (INN)



Systematic (IUPAC) name	
?-(2-Oxopyrrolidin-1-yl)butanamide	
Clinical data	
Pronunciation	/lɛvɪtɪˈræsɪtæm/
AHFS/Drugs.com	monograph
MedlinePlus	a699059
Licence data	US FDA;link
Pregnancy category	AU: B3 US: C (Risk not ruled out)
Legal status	AU: Prescription Only (S4) US: ℞-only ℞ (Prescription only)
Routes of administration	Oral, intravenous
Pharmacokinetic data	
Bioavailability	~100%
Protein binding	<10%
Metabolism	Enzymatic hydrolysis of acetamide group

Biological half-life	6 - 8 hr
Excretion	Urinary
Identifiers	
CAS Registry Number	102767-28-2 ✓
ATC code	N03AX14
PubChem	CID: 5284583
IUPHAR/BPS	6826
DrugBank	DB01202 ✗
UNII	44YRR34555 ✓
KEGG	D00709 ✓
ChEBI	CHEBI:6437 ✗
ChEMBL	CHEMBL1286 ✓
Chemical data	
Formula	$C_8H_{14}N_2O_2$
Molecular mass	170.209 g/mol
SMILES[show]	
InChI[show]	
✗ **(what is this?)** **(verify)**	

Levetiracetam, marketed under the trade name **Keppra** among others, is a medication used to treat epilepsy.[1] It is used for partial onset, myoclonic, or tonic-clonic seizures.[2] It is the S-enantiomer of etiracetam.

Levetiracetam is available orally in two forms: immediate release and extended release.[3] An immediate release tablet has been available as a generic in the United States since November 2008, and in the UK since 2011.[4][5] The United States patent for the extended release tablet expires September 17, 2028.[6]

Contents

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Medical uses[edit]

Levetiracetam has been approved in the United States as add-on treatment for partial (focal), myoclonic, and tonic-clonic seizures.[2]Levetiracetam has been approved in the European Union as a monotherapy treatment for epilepsy in the case of partial seizures, or as an adjunctive therapy for partial, myoclonic, and tonic-clonic seizures.[7] Levetiracetam has been shown to reduce partial (focal) seizures by 50% or more as an add-on medication.[5] It is also used in veterinary medicine for similar purposes.

Levetiracetam is sometimes used off-label to treat status epilepticus[8][9] or to prevent seizures associated with subarachnoid hemorrhages.[10]

Levetiracetam has potential benefits for other psychiatric and neurologic conditions such as Tourette syndrome,[11] anxiety disorder,[12] and Alzheimer's disease.[13] However, its most serious adverse effects are behavioral, and its benefit-risk ratio in these conditions is not well understood.[12]

Levetiracetam has not been found to be useful for treatment of neuropathic pain,[14] nor for treatment of essential tremors.[15]Levetiracetam has not been found to be useful for treating autism,[16][17] but is an effective treatment for partial, myoclonic, or tonic-clonic seizures associated with autism spectrum disorder.[18]

Pregnancy[edit]

Levetiracetam is a Pregnancy Category C Drug. Studies in female pregnant rats have shown minor fetal skeletal abnormalities when given maximum recommended human doses of levetiracetam orally throughout pregnancy and lactation.[14]

Elderly[edit]

Studies were conducted to look for increased adverse effects in the elderly population as compared to younger patients. One such study published in Epilepsy Research showed no significant increase in incidence of adverse symptoms experienced by young or elderly patients with central nervous system (CNS) disorders.[16]

Children[edit]

Levetiracetam may be used in children depending on age and type of seizure. Animal studies in juvenile rats and dogs did not demonstrate a potential for age-specific toxicity.[2]

Kidney impairment[edit]

Kidney impairment decreases the rate of elimination of levetiracetam from the body. Individuals with reduced kidney function may require dose adjustments. Kidney function can be estimated from the rate of creatinine clearance.[3]

Liver impairment[edit]

Dose adjustment of levetiracetam is not necessary in liver impairment.[3]

Adverse effects[edit]

The most common adverse effects of levetiracetam treatment include CNS effects such as somnolence, decreased energy, headache, dizziness, and coordination difficulties. These adverse effects are most pronounced in the first month of therapy. About 4% of patients dropped out of pre-approval clinical trials due to these side effects.[3]

About 13% of people taking levetiracetam experience adverse neuropsychiatric symptoms, which are usually mild. These include agitation, hostility, apathy, anxiety, emotional lability, and depression. Serious psychiatric adverse side effects that are reversed by drug discontinuation occur in about 1%. These include hallucinations, suicidal thoughts, or psychosis. These occurred mostly within the first month of therapy, but they could develop at any time during treatment.[19]

A study published in 2005 suggests that the addition of pyridoxine (vitamin B6) may reduce some of the psychiatric symptoms.[20]

Although rare, Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which appears as a painful spreading rash with redness and blistering and/or peeling skin, have been reported in patients treated with levetiracetam.[21] The incidence of SJS following exposure to anti-epileptics such as levetiracetam is about 1 in 3,000.[22]

Levetiracetam should not be used in people who have previously shown hypersensitivity to levetiracetam or any of the inactive ingredients in the tablet or oral solution. Such hypersensitivity reactions include, but are not limited to, unexplained rash with redness or blistered skin, difficulty breathing, and tightness in the chest or airways.[3]

Suicide[edit]

Levetiracetam, along with other anti-epileptic drugs, can increase the risk of suicide behavior or thoughts. People taking levetiracetam should be monitored closely for signs of worsening depression, suicidal thoughts or tendencies, or any altered emotional or behavioral states.[2]

Drug interactions[edit]

No significant pharmacokinetic interactions were observed between levetiracetam or its major metabolite and concomitant medications.[23] The pharmacokinetic profile of levetiracetam is not influenced by phenytoin, phenobarbital, primidone, carbamazepine, valproic acid, lamotrigine, gabapentin, digoxin, oral contraceptives ethinylestradiol, or warfarin.[24]

Mechanism of action[edit]

The exact mechanism by which levetiracetam acts to treat epilepsy is unknown. However, the drug binds to a synaptic vesicle glycoprotein, SV2A,[25] and inhibits presynaptic calcium channels[26] reducing neurotransmitter release and acting as a neuromodulator. This is believed to impede impulse conduction across synapses.[27]

Pharmacokinetics[edit]

Absorption[edit]

The absorption of levetiracetam tablets and oral solution is rapid and essentially complete. The bioavailability of levetiracetam is close to 100 percent, and the effect of food on absorption is minor.[3]

Distribution[edit]

The volume of distribution of levetiracetam is similar to total body water. Levetiracetam modestly binds to plasma proteins (less than 10%).[3]

Metabolism[edit]

Levetiracetam does not undergo extensive metabolism, and the metabolites formed are not active and do not exert pharmacological activity. Metabolism of levetiracetam is not by liver cytochrome P450 enzymes, but through other metabolic pathways such as hydrolysis and hydroxylation.[3]

Excretion[edit]

Levetiracetam is eliminated from the body primarily by the kidneys with about 66 percent of the original drug passed unchanged into urine. The plasma half-life of levetiracetam in adults is about 6 to 8 hours.[3]

Available forms[edit]

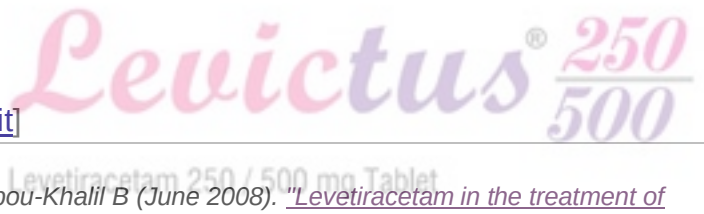
Levetiracetam is available as regular and extended release oral formulations and as intravenous formulations.[3][28]

The branded version Keppra is manufactured by UCB Pharmaceuticals Inc.[29]

In 2015 Aprecia's 3d-printed form of the drug was approved by the FDA.[30]

See also[edit]

- Racetams



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