MedChoice™
CNS

Levetiracetam

Rx

Kepdin®

500 mg Film-Coated Tablet
ANTIEPILEPTIC

FORMULATION:
Each film-coated tablet contains :
Levetiracetam USP ..... 500 mg

PRODUCT DESCRIPTION:
Levetiracetam (Kepdin) 500 mg ..... White, elongated, biconvex, plain on both side and film-coated tablets.

PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: antiepileptics, other antiepileptics
The active substance, levetiracetam, is a pyrrolidone derivative (S-enantiomer of α-ethyl-2-oxo-1-pyrrolidine acetamide), chemically unrelated to existing antiepileptic active substances.

Mechanism of action
The mechanism of action of levetiracetam still remains to be fully elucidated. *In vitro* and *in vivo* experiments suggest that levetiracetam does not alter basic cell characteristics and normal neurotransmission.
In vitro studies show that levetiracetam affects intraneuronal Ca2+ levels by partial inhibition of N-type Ca2+ currents and by reducing the release of Ca2+ from intraneuronal stores. In addition, it partially reverses the reductions in GABA- and glycine-gated currents induced by zinc and β-carbolines. Furthermore, levetiracetam has been shown in *in vitro* studies to bind to a specific site in rodent brain tissue. This binding site is the synaptic vesicle protein 2A, believed to be involved in vesicle fusion and neurotransmitter exocytosis. Levetiracetam and related analogs show a rank order of affinity for binding to the synaptic vesicle protein 2A which correlates with the potency of their anti-seizure protection in the mouse audiogenic model of epilepsy. This finding suggests that the interaction between levetiracetam and the synaptic vesicle protein 2A seems to contribute to the antiepileptic mechanism of action of the medicinal product.

Pharmacodynamic effects
Levetiracetam induces seizure protection in a broad range of animal models of partial and primary generalised seizures without having a pro-convulsant effect. The primary metabolite is inactive.
In man, an activity in both partial and generalised epilepsy conditions (epileptiform discharge/photoparoxysmal response) has confirmed the broad spectrum pharmacological profile of Levetiracetam.

Clinical efficacy and safety
Adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults, adolescents, children and infants from 1 month of age with epilepsy.
In adults, levetiracetam efficacy has been demonstrated in 3 double-blind, placebo-controlled studies at 1000 mg, 2000 mg, or 3000 mg/day, given in 2 divided doses, with a treatment duration of up to 18 weeks. In a pooled analysis, the percentage of patients who achieved 50 % or greater reduction from baseline in the partial onset seizure frequency per week at stable dose (12/14 weeks) was of 27.7 %, 31.6 % and 41.3 % for patients on 1000, 2000 or 3000 mg levetiracetam respectively and of 12.6 % for patients on placebo.

PHARMACOKINETICS:
Absorption of levetiracetam with peak plasma concentrations occurring in about an hour following oral administration in fasted subjects. The oral bioavailability of levetiracetam tablet is 100% and the tablet and oral solution are bioequivalent in rate and extent of absorption. Food does not affect the extent of absorption of levetiracetam but it decreases Cmax by 20% and delays Tmax by 1.5 hours. Levetiracetam is not extensively metabolized in humans. The major metabolic pathway is the enzymatic hydrolysis of the acetamide group, which produces the carboxylic acid, ucb L057 (24% of dose) and is not dependent on any liver cytochrome P450 isoenzymes. Levetiracetam plasma half-life in adults is 7 ± 1 hour and is unaffected by either dose or repeated administration. Levetiracetam is eliminated from the systemic circulation by renal excretion as unchanged drug which represents 66% of administered dose.

INDICATIONS:
Levetiracetam is used as an adjunct in the treatment of partial seizures with or without secondary generalizations, myoclonic seizures, and primary generalized tonic-clonic seizures.

DOSAGE AND ADMINISTRATION:
Partial Onset Seizures:
Adults 16 years and older-initial daily dose of 1000 mg/day given as twice-daily dosing (500 mg twice daily).
1 month to < 6 months-initial daily dose of 14 mg/kg in two divided doses (7 mg/kg twice daily).
6 months to < 4 years-initial daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). The daily dose should be increased in 2 weeks by an increment of 20 mg/kg to the recommended daily dose of 50 mg/kg (25 mg/kg twice daily)
4 years to <16 years-initial daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). The daily dose should be increased every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 mg/kg twice daily).

Myoclonic Seizures in patients 12 years of age and older:
Treatment should be initiated with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Dosage should be increased by 1000 mg/day every 2 weeks to the recommended daily dose of 3000 mg.

Primary generalized tonic-clonic seizures:
Adult 16 years and older – treatments should be initiated with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily).
Pediatric patients ages 6 to < 16 years – treatment should be initiated with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily).
Or as prescribed by the physician.

CONTRAINDICATIONS:
Hypersensitivity to the active substance, other pyrrolidone derivatives or to any of the excipients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Renal impairment
The administration of levetiracetam to patients with renal impairment may require dose adjustment. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection.

Acute kidney injury
The use of levetiracetam has been very rarely associated with acute kidney injury, with a time to onset ranging from a few days to several months.

Blood cell counts
Rare cases of decreased blood cell counts (neutropenia, agranulocytosis, leucopenia, thrombocytopenia and pancytopenia) have been described in association with levetiracetam administration, generally at the beginning of the treatment. Complete blood cell counts are advised in patients experiencing important weakness, pyrexia, recurrent infections or coagulation disorders.

Suicide
Suicide, suicide attempt, suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents (including levetiracetam. A meta-analysis of randomized placebo-controlled trials of antiepileptic medicinal products has shown a small increased risk of suicidal thoughts and behaviour. The mechanism of this risk is not known.

Therefore, patients should be monitored for signs of depression and/or suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of depression and/or suicidal ideation or behaviour emerge.

Pediatric population
The tablet formulation is not adapted for use in infants and children under the age of 6 years.

Available data in children did not suggest impact on growth and puberty. However, long term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children remain unknown.

PRECAUTIONS:
Levetiracetam should be used with caution and in reduced doses in patients with renal impairment, those undergoing hemodialysis and in patients with severe hepatic impairment.

Breastfeeding: Levetiracetam is transferred into breast milk in significant amounts, but serum concentrations in breastfed infants are very low.

Pregnancy: The management of epilepsy during pregnancy may present problems for both the mother and the fetus. Evidence for any effect of the newer antiepileptic on the fetus is particularly scanty. Limited data have not so far suggested a significant increase in risk with levetiracetam.

ADVERSE DRUG REACTIONS:
The most common adverse effects associated with levetiracetam are somnolence, weakness and dizziness. Anorexia, diarrhea, dyspepsia, nausea, ataxia, headache, amnesia, depression, emotional liability, insomnia, nervousness, tremor, vertigo, diplopia and rash may occur less frequently. A raised incidence of mild infections, such as the common cold and upper respiratory-tract infections has been reported.
Other effects reported include abnormal behavior, aggression, anger, anxiety, confusion, hallucinations, irritability, psychotic disorders, neutropenia, pancytopenia and thrombocytopenia.

DRUG INTERACTIONS:
Potential pharmacokinetic interactions with levetiracetam were assessed in clinical pharmacokinetic studies (phenytoin, valproate, warfarin, digoxin, oral contraceptive, probenecid) and through pharmacokinetic screening in the placebo-controlled clinical studies in epileptic patients. Symptoms of carbamazepine toxicity have been reported when levetiracetam was added to carbamazepine therapy; this interaction appeared to be due to pharmacodynamics mechanism as blood levels of carbamazepine and its metabolites were not altered.

OVERDOSE AND TREATMENT:
Symptoms
Somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed with levetiracetam overdoses.

Management of overdose
After an acute overdose, the stomach may be emptied by gastric lavage or by induction of emesis. There is no specific antidote for levetiracetam. Treatment of an overdose will be symptomatic and may include hemodialysis. The dialyser extraction efficiency is 60 % for levetiracetam and 74 % for the primary metabolite.

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction."

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

Keep all medicines out of children's reach.

AVAILABILITY:
Levetiracetam (Kepdin) 500 mg Film-Coated Tablet .....Alu/Alu Blister Pack x10's (Box of 10 Tablets)

DRP-4583-01
Date of First Authorization: August 06, 2015
Date of Renewal of Authorization: June 19, 2019
Date of Revision of Package Insert: April 01, 2020

Manufactured by:
AKUMS DRUGS & PHARMACEUTICALS LTD.
(Plant-I Solid Oral Dosage Facility)
Plot No.: 19, 20, 21, Sector-6A, I.I.E., SIDCUL, Ranipur,
Haridwar-249403, Uttarakhand, India

Manufactured for:
UNOSOURCE PHARMA LTD.
503 / 504, 5th Floor, Hubtown Solaris, N.S. Phadke
Marg, Andheri (East), Mumbai-400069, India

Imported by:
AMBICA INTERNATIONAL CORPORATION
9 Amsterdam Extension, Merville Park Subd.,
Parañaque City, Philippines

Distributed by:
MEDCHOICE CNS PHARMA CORPORATION
10F Unit 1001, 88 Corporate Center, Sedeño cor. Valero
Sts., Salcedo Village, Makati City, Metro Manila

MedChoice
CNS

Levetiracetam

Kepdin

250 mg Film-Coated Tablet • **500** mg Film-Coated Tablet

ANTICONVULSANT

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Levetiracetam ..... 250 mg

Each film-coated tablet contains :
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STORAGE CONDITION:
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KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

AVAILABILITY:
Levetiracetam (Kepdin) 250 mg Film-Coated Tablet .....Alu/Alu Blister Pack of 10's (Box of 10 Tablets)

AVAILABILITY:
Levetiracetam (kepdin) 500 mg Film-Coated Tablet .....Alu/Alu Blister Pack of 10's (Box of 10 Tablets).

Levetiracetam (Kepdin) 250 mg
DRP-4585-01
Date of First Authorization: August 06, 2015
Date of Renewal of Authorization:

Levetiracetam (Kepdin) 500 mg
DRP-4583-01
Date of First Authorization : August 06, 2015
Date of Renewal of Authorization: June 19, 2019

Date of Revision of Package Insert : September 6, 2019

Manufactured by:
AKUMS DRUGS & PHARMACEUTICALS LTD.
19-21, Sector-6A, I.I.E. Sidcul,
Ranipur, Haridwar-249403, India

Manufactured for:
UNOSOURCE PHARMA LTD.
503 / 504, 5th Floor, Hubtown Solaris, N.S. Phadke
Marg, Andheri (East), Mumbai-400069, India

Imported by:
AMBICA INTERNATIONAL CORPORATION
No. 9 Amsterdam Extn., Merville Park Subd.,
Parañaque City, Philippines

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MEDCHOICE CNS PHARMA CORPORATION
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