FITZLOC TABLET
(Levetiracetam)

COMPOSITION:

FITZLOC 250mg Tablet
Each film coated tablet contains:
Levetiracetam ……250mg

FITZLOC 500mg Tablet
Each film coated tablet contains:
Levetiracetam ……500mg

FITZLOC 750mg Tablet
Each film coated tablet contains:
Levetiracetam ……750mg

DESCRIPTION:

The chemical name of levetiracetam, a single enantiomer, is (-)-(S)-α-ethyl-2-oxo-1-pyrrolidine acetamide, its molecular formula is $C_8H_{14}N_2O_2$ and its molecular weight is 170.21.

PHARMACOLOGICAL ACTIONS:

Pharmacodynamic properties:

The precise mechanism(s) by which levetiracetam exerts its antiepileptic effect is unknown, levetiracetam inhibits burst firing without affecting normal neuronal excitability, suggesting that levetiracetam may selectively prevent hypersynchronization of epileptiform burst firing and propagation of seizure activity.

Pharmacokinetic properties:

Absorption and Distribution

Absorption of levetiracetam is rapid, with peak plasma concentrations occurring in about an hour following oral administration in fasted subjects. The oral bioavailability of levetiracetam tablets is 100%. Food does not affect the extent of absorption of levetiracetam but it decreases C_{max} by 20% and delays T_{max} by 1.5 hours. The pharmacokinetics of levetiracetam are linear over the dose range of 500-5000 mg. Steady state is achieved after 2 days of multiple twice-daily dosing. Levetiracetam and its major metabolite are less than 10% bound to plasma proteins.

Metabolism

Levetiracetam is not extensively metabolised; about 25% of a dose is metabolised by hydroxylation to inactive metabolites.

Elimination
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. The total body clearance is 0.96 mL/min/kg and the renal clearance is 0.6 mL/min/kg. The mechanism of excretion is glomerular filtration with subsequent partial tubular reabsorption.
Levetiracetam clearance is reduced in patients with impaired renal function.

INDICATIONS AND USAGE:

Levetiracetam is an antiepileptic drug indicated for adjunctive therapy in the treatment of:

• Partial onset seizures in patients one month of age and older with epilepsy
• Myoclonic seizures in patients 12 years of age and older with juvenile myoclonic epilepsy
• Primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy.

DOSAGE AND ADMINISTRATION:

Partial Onset Seizures:
Adults 16 Years and Older
Treatment should be initiated with a daily dose of 1000 mg/day, given as twice-daily dosing (500 mg BID). Additional dosing increments may be given (500 mg twice a day adding every 2 weeks) to a maximum recommended daily dose of 3000 mg/day.
Pediatric Patients: Ages 4 To <16 Years
For pediatric patients weighing 20 to 40 kg, treatment should be initiated with a daily dose of 500 mg given as twice daily dosing (250 mg twice daily). The daily dose should be increased every 2 weeks by increments of 500 mg to a maximum recommended daily dose of 1500 mg (750 mg twice daily).
For pediatric patients weighing more than 40 kg, treatment should be initiated with a daily dose of 1000 mg/day given as twice daily dosing (500 mg twice daily). The daily dose should be increased every 2 weeks by increments of 1000 mg/day to a maximum recommended daily dose of 3000 mg/day (1500 mg twice daily).

Myoclonic Seizures in Patients 12 Years of Age and Older With Juvenile Myoclonic Epilepsy:
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/day. The effectiveness of doses lower than 3000 mg/day has not been studied.

Primary Generalized Tonic-Clonic Seizures:

Adults 16 Years 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/day.

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). 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). Levetiracetam tablet is to be used in patients with body weight above 20, only whole tablets should be administered.

Adult Patients with Impaired Renal Function

Levetiracetam dosing must be individualized according to the patient's renal function status. Recommended doses and adjustment for dose for adults are shown in Table 1.

Cr.Cl.	50 to 79 mL/minute	1 to 2 g
Cr.Cl.	30 to 49 mL/minute	500 mg to 1.5 g
Cr.Cl.	less than 30 mL/minute	500 mg to 1 g

Patients receiving dialysis may be given a loading dose of 750 mg when starting levetiracetam followed by doses of 500 mg to 1 g once daily; a supplemental dose of 250 to 500 mg is recommended after dialysis.

CONTRAINDICATIONS:

Hypersensitivity to any component of this product.

ADVERSE EFFECTS:

The most commonly reported adverse effects associated with levetiracetam are somnolence, weakness, and dizziness. Anorexia, diarrhoea, dyspepsia, nausea, weight gain or loss, myalgia, ataxia, headache, amnesia, depression, emotional lability, insomnia, nervousness, tremor, vertigo, diplopia, and rash may occur less frequently.

PRECAUTIONS:

Behavioral abnormalities: The psychiatric signs symptoms like behavioral abnormalities (aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, hyperkinesias, irritability, nervousness, neurosis, and personality disorder) should be monitored.

Suicidal Behavior: Patients treated with any antiepileptic drugs for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Signs and symptoms of somnolence and fatigue: Patients should be monitored for signs and symptoms of somnolence and fatigue and advised not to drive or operate machinery until they have gained sufficient experience on levetiracetam to gauge whether it adversely affects their ability to drive or operate machinery.

Skin reactions: Levetiracetam should be discontinued if serious skin reactions like rash appear, unless the rash is clearly not drug-related. If signs or symptoms of skin reactions persist, use of Levetiracetam should not be resumed.
Withdrawal Seizures: Antiepileptic drugs, including levetiracetam, should be withdrawn gradually to minimize the potential of increased seizure frequency.
Geriatric Use: Elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function
Use in Patients with Impaired Renal Function: Clearance of levetiracetam is decreased in patients with renal impairment and is correlated with creatinine clearance. Dose adjustment is recommended for patients with impaired renal function and supplemental doses should be given to patients after dialysis.
Pregnancy:
There are no adequate and well-controlled studies in pregnant women. Levetiracetam should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Lactation:
Levetiracetam is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

DRUG INTERACTIONS:

No significant pharmacokinetic interactions were observed between levetiracetam or its major metabolite and concomitant medications via human liver cytochrome P450 isoforms, epoxide hydrolase, UDP-glucuronidation enzymes, P-glycoprotein, or renal tubular secretion.

OVERDOSAGE:

The highest known dose reported of levetiracetam was 6000 mg/day. Other than drowsiness, there were no adverse events reported. Cases of somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed with levetiracetam overdoses in postmarketing use.
There is no specific antidote for overdose with levetiracetam. If indicated, elimination of unabsorbed drug should be attempted by emesis or gastric lavage.

INSTRUCTIONS:

- To be sold on the prescription of a registered medical practitioner only.
- Store at 25°C.
- Protect from moisture and sunlight.
- Keep out of the reach of children.

MANUFACTURED BY:

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