Recetam®
(Levetiracetam)

250mg, 500mg, Tablets U.S.P.
100mg/mL Oral Solution U.S.P.
500mg/5mL Injection U.S.P.

ریسی ٹیم
(لیویٹی راسیٹیم)

۲۵۰ ایم جی/۵۰۰ ایم جی گولیاں یو۔ایس۔پی
اورل سلوشن ۱۰۰ ایم جی/ایم ایل یو۔ایس۔پی
انجکشن ۵۰۰ ایم جی/ایم ایل یو۔ایس۔پی

صرف پرچہ پر تجویز کے

QUALITATIVE AND QUANTITATIVE COMPOSITION

Recetam® Tablets 250mg: Each film-coated tablet contains: Levetiracetam U.S.P.....250mg
Recetam® Tablets 500mg: Each film-coated tablet contains: Levetiracetam U.S.P.....500mg
Recetam® Oral Solution 100mg/mL: Each mL contains: Levetiracetam U.S.P.....100mg
Recetam® Injection 500mg/5mL: Each 5mL contains: Levetiracetam U.S.P. 500mg

DESCRIPTION: Recetam is an antiepileptic drug. The chemical name of levetiracetam, a single enantiomer, is (-)-(S)-α-ethyl-2-oxo-1-pyrrolidine acetamide, its molecular formula is C8H14N2O2 and its molecular weight is 170.21.

CLINICAL PHARMACOLOGY: Mechanism of Action: The precise mechanism(s) by which levetiracetam exerts its antiepileptic effect is unknown. Levetiracetam did not inhibit single seizures induced by maximal stimulation with electrical current or different chemoconvulsants and showed only minimal activity in submaximal stimulation and in threshold tests.

Pharmacodynamics: Effects on QTc Interval: There is no evidence of significant QTc prolongation. **Pharmacokinetics: Absorption and Distribution:** Levetiracetam is almost completely absorbed after oral administration. The oral bioavailability of levetiracetam tablets, oral solution and infusion are bioequivalent, as well as, the bioavailability of extended release tablet is similar to the immediate release tablets. Levetiracetam and its major metabolite are less than 10% bound to plasma proteins. Plasma half-life of Levetiracetam across studies is approximately 6-8 hours, whereas in extended release it is approximately 7 hours.

Metabolism: Levetiracetam is not extensively metabolized in humans. The major metabolic pathway is the enzymatic hydrolysis of the acetamide group, which produces the carboxylic acid metabolite, ucb L057 (24% of dose) and is not dependent on any liver cytochrome P450 isoenzymes. The major metabolite is inactive in animal seizure models. Two minor metabolites were identified as the product of hydroxylation of the 2-oxo-pyrrolidine ring (2% of dose) and opening of the 2-oxo-pyrrolidine ring in position 5 (1% of dose). There is no enantiomeric interconversion of levetiracetam or its major metabolite. **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. The metabolite ucb L057 is excreted by glomerular filtration and active tubular secretion with a renal clearance of 4 mL/min/kg. Levetiracetam elimination is correlated to creatinine clearance. Levetiracetam clearance is reduced in patients with renal impairment.

INDICATIONS AND USAGE: Recetam Tablet, oral solution and Infusion are indicated for the treatment of Partial Onset Seizures, Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy and Primary Generalized Tonic-Clonic Seizures.

Contraindications: Recetam is contraindicated in patients with a hypersensitivity to levetiracetam. Reactions have included anaphylaxis and angioedema.

INTERACTIONS: DRUG INTERACTIONS : Probenecid: Renal clearance of Levetiracetam metabolite (ucb L057) in the presence of probenecid decreases 60%. **Methotrexate:** Levetiracetam decreases the clearance of methotrexate. (Severe)

USE IN SPECIFIC POPULATION: Pregnancy: Pregnancy Category C: Recetam should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breast Feeding: Levetiracetam is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Recetam, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** The safety and effectiveness of Recetam in the adjunctive treatment of partial onset seizures in pediatric patients age 1 month to 16 years with epilepsy have been established. The dosing recommendation in these pediatric patients varies according to age group and is weight-based. **Geriatric Use:** Care should be taken in dose selection, and it may be useful to monitor renal function. **Renal Impairment:** Dosage adjustment is recommended for patients with impaired renal function and supplemental doses should be given to patients after dialysis.

PRECAUTIONS: Behavioral Abnormalities and Psychotic Symptoms: Recetam may cause behavioral abnormalities and psychotic symptoms. Patients treated should be monitored. **Somnolence, Fatigue and Coordination Difficulties:** Patients should be monitored for somnolence and fatigue, and be advised not to drive or operate machinery until they have gained sufficient experience on Recetam to gauge whether it adversely affects their ability to drive or operate machinery. **Anaphylaxis and Angioedema:** Recetam can cause anaphylaxis or angioedema after the first dose or at any time during treatment. Signs and symptoms included hypotension, hives, rash, respiratory distress, and swelling of the face, lip, mouth, eye, tongue, throat, and feet. Recetam should be discontinued and the patient should seek immediate medical attention. Recetam should be discontinued permanently if a clear alternative etiology for the reaction cannot be established. **Serious Dermatological Reactions:** Includes Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in both pediatric and adult patients. Recetam should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered. **Withdrawal Seizures:** Antiepileptic drugs, including Recetam, should be withdrawn gradually to minimize the potential of increased seizure frequency. **Hematologic Abnormalities:** Cases of agranulocytosis, pancytopenia, and thrombocytopenia have been reported in the postmarketing setting. A complete blood count is recommended in patients experiencing significant weakness, pyrexia, recurrent infections, or coagulation disorders. **Increase in Blood Pressure:** Monitor patients 1 month to <4 years of age for increases in diastolic blood pressure. **Seizure Control During Pregnancy:** Physiological changes may gradually decrease plasma levels of levetiracetam throughout pregnancy. This decrease is more pronounced during the third trimester. Close monitoring should continue through the postpartum period especially if the dose was changed during pregnancy.

DOSAGE AND ADMINISTRATION: Recetam is given orally with or without food. The dosing regimen depends on the indication, age group, dosage form (tablets or oral solution), and renal function. Recetam tablets should be swallowed whole. Oral solution for pediatric patients with body weight ≤ 20 kg. Prescribe the oral solution or tablets for pediatric patients with body weight above 20 kg. When using the oral solution in pediatric patients, dosing is weight-based (mg per kg) using a calibrated measuring device. For administration of oral solution, requisite dose may be diluted in a glass of water. Recetam Tablet XR is administered once daily. Recetam infusion is for intravenous use only and should be diluted in 100 mL of a compatible diluent prior to administration. If a smaller volume is required (e.g. pediatric patients), the amount of diluent should be calculated to not exceed a maximum levetiracetam concentration of 15 mg per mL of diluted solution. Consideration should also be given to the total daily fluid intake of the patient. Recetam infusion should be administered as a 15-minute IV infusion. The compatible diluents are glucose 5% or 0.9% Sodium Chloride. **Monotherapy of focal seizures with or without secondary generalisation** • BY MOUTH, OR BY INTRAVENOUS INFUSION **Child 16–17 years:** Initially 250 mg once daily for 1 week, then increased to 250 mg twice daily, then increased in steps of 250 mg twice daily (max. per dose 1.5 g twice daily), adjusted according to response, dose to be increased every 2 weeks. • **Adult:** Initially 250 mg once daily for 1–2 weeks, then increased to 250 mg twice daily, then increased in steps of 250 mg twice daily (max. per dose 1.5 g twice daily), adjusted according to response, dose to be increased every 2 weeks. Adjunctive therapy of focal seizures with or without secondary generalisation • BY MOUTH • **Child 1–5 months:** Initially 7 mg/kg once daily, then increased

in steps of up to 7 mg/kg twice daily (max. per dose 21 mg/kg twice daily), dose to be increased every 2 weeks

• **Child 6 months–17 years (body-weight up to 50 kg):** Initially 10 mg/kg once daily, then increased in steps of up to 10 mg/kg twice daily (max. per dose 30 mg/kg twice daily), dose to be increased every 2 weeks • **Child 12–17 years (body-weight 50 kg and above):** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2–4 weeks • **Adult:** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2–4 weeks • BY INTRAVENOUS INFUSION • **Child 4–17 years (body-weight up to 50 kg):** Initially 10 mg/kg once daily, then increased in steps of up to 10 mg/kg twice daily (max. per dose 30 mg/kg twice daily), dose to be increased every 2 weeks. • **Child 12–17 years (body-weight 50 kg and above):** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2 weeks. • **Adult:** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2–4 weeks. Adjunctive therapy of myoclonic seizures and tonic-clonic seizures. • **BY MOUTH, OR BY INTRAVENOUS INFUSION • Child 12–17 years (body-weight up to 50 kg):** Initially 10 mg/kg once daily, then increased in steps of up to 10 mg/kg twice daily (max. per dose 30 mg/kg twice daily), dose to be increased every 2 weeks

• **Child 12–17 years (body-weight 50 kg and above):** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2 weeks. • **Adult:** Initially 250 mg twice daily, then increased in steps of 500 mg twice daily (max. per dose 1.5 g twice daily), dose to be increased every 2–4 weeks

Dosage Adjustment Regimen of Recetam Tablets, oral Solution and Recetam Infusion For Adult Patients With Renal

Group	Creatinine Clearance (mL/min/1.73m²)	Dosage (mg)	Frequency
Normal	> 80	500 to 1,500	Every 12 hours
Mild	50-80	500 to 1,000	Every 12 hours
Moderate	30-50	250 to 750	Every 12 hours
Severe	<30	250 to 500	Every 12 hours
ESRD patients using dialysis	----	500 to 1,000*	Every 24 hours

*Following Dialysis, a 250 to 500mg supplement dose is recommended.

HEPATIC IMPAIRMENT: Dose adjustments • In adults Halve dose in severe hepatic impairment if eGFR less than 60 mL/minute/1.73m2. • In children Halve dose in severe hepatic impairment if estimated glomerular filtration rate less than 60 mL/minute/1.73m2.

OVERDOSE: Signs, Symptoms and Laboratory Findings of Acute Overdosage in Humans: Cases of somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed. **Management of Overdose:** There is no specific antidote for overdose with Recetam. If indicated, elimination of unabsorbed drug should be attempted by emesis or gastric lavage; usual precautions should be observed to maintain airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the patient's clinical status. **Hemodialysis:** Standard hemodialysis procedures result in significant clearance of levetiracetam (approximately 50% in 4 hours) and should be considered in cases of overdose. Although hemodialysis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal impairment.

ADVERSE REACTIONS: - Common or very common: Anxiety. appetite decreased. asthenia. behaviour abnormal. cough. depression. diarrhoea. dizziness. drowsiness. gastrointestinal discomfort. headache. increased risk of infection. insomnia. mood altered. movement disorders. nausea .skin reactions. vertigo. vomiting. • **Uncommon:** Alopecia. concentration impaired. confusion. hallucination. leukopenia. muscle weakness. myalgia. paraesthesia. psychotic disorder. suicidal tendencies. thrombocytopenia. vision disorders. weight changes • **Rare or very rare:** Acute kidney injury. agranulocytosis. hepatic disorders. hyponatraemia. neutropenia. pancreatitis. pancytopenia. personality disorder. rhabdomyolysis. severe cutaneous adverse reactions(SCARs). thinking abnormal . The most common side effects seen in children, in addition to those listed above: tiredness, acting aggressive, nasal congestion, decreased appetite, irritability. These side effects can happen at any time but happen more often within the first 4 weeks of treatment except for infection.

INSTRUCTIONS: For Tablets and Oral Solution: Dosage as directed by the physician. Store below 30°C. Protect from heat light and moisture. **For Injection:** Store below 30°C. Protect from sunlight. Keep all medicines out of the reach of children.

Must be diluted prior to administration. Injection should not be used if container is leaking, solution is cloudy or it contains undissolved particles. Any unused portion of the Recetam injection contents should be discarded. Recetam injection may be mixed with the diluents and antiepileptic drugs. The diluted solution should not be stored for more than 4 hours at controlled room temperature [15-30ºC].

PRESENTATION: Recetam (Levetiracetam) Tablets 250 mg are available in Alu-Alu blister pack of 10's along with insert. Recetam (Levetiracetam) Tablets 500 mg are available in Alu-Alu blister pack of 10's along with insert.

Recetam (Levetiracetam) Oral solution 100 mg/mL is available in 60mL Amber PET bottle along with dropper and insert. Recetam (Levetiracetam) Injection 500mg/5mL is available 1x5mL Ampoule along with insert.

علامات/طریقہ استعمال: ریسی ٹیم ٹیبلٹس، اورل سلوشن اور انجکشن جزوی اور عمومی مرگی کے دوروں کے علاج کے لئے تجویز کردہ ہے۔

مضر اثرات: بے چینی، بھوک میں کمی، کھانسی، ذہنی دباؤ، سر درد، ہیضہ کی کمی، متلی، چکر آنا اور تھکاوٹ۔

احتیاطی تدابیر: حاملہ خواتین اور دودھ پلانے والی مائیں صرف مستند ڈاکٹر کے مشورے سے استعمال کریں۔

بچوں کی دوا دور اور محفوظ جگہ پر رکھیں۔ بزرگوں میں ریسی ٹیم کا استعمال احتیاط سے کریں۔

جگر اور گردے کے مریضوں میں دوا کا استعمال ڈاکٹر کے مشورے سے کریں۔ مریض میں اینافائلیکسز اور ہائپوناٹریمیا کی علامات ظاہر ہوتے ہی ریسی ٹیم کا استعمال روک دیں۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ٹیبلٹس اور اورل سلوشن: ۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔

روشنی، گرمی اور نمی سے محفوظ رکھیں۔

انجکشن: ۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔ سورج کی روشنی سے محفوظ رکھیں۔

تیار شدہ محلول ۱۵ سے ۳۰ ڈگری سینٹی گریڈ پر ۴ گھنٹوں سے زائد نہ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

غیر استعمال شدہ محلول کو ضائع کردیں۔ انجکشن کے ایک محلول کے دھندلا ہونے یا کسی بھی قسم کی غیر معمولی پریشانی نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔ استعمال سے پہلے انجکشن کو مزید ڈائیلیوٹ کرلیں۔

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