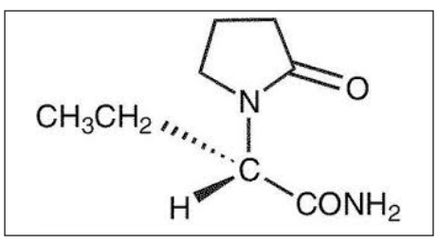
Emscot Tablets

ایم سکاٹ ٹیبلٹس

COMPOSITION:
Each film coated tablet contains: Levetiracetam USP…… 250, 500 & 750 mg

DESCRIPTION
EMSCOT is an antiepileptic drug available as 250 mg , 500 mg and 750 mg . 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. Levetiracetam is chemically unrelated to existing antiepileptic drugs (AEDs). It has the following structural formula:



CLINICAL PHARMACOLOGY
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.
Pharmacokinetics:
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 Cmax by 20% and delays Tmax 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.
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.
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
- ***Partial Onset Seizures:*** EMSCOT is indicated as adjunctive therapy in the treatment of partial onset seizures in adults and children 1 month of age and older with epilepsy.
- ***Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy:*** EMSCOT is indicated as adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents 12 years of age and older with juvenile myoclonic epilepsy.
- ***Primary Generalized Tonic-Clonic Seizures:*** EMSCOT is indicated as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in adults and children 6 years of age and older with idiopathic generalized epilepsy.

CONTRAINDICATIONS
EMSCOT is contraindicated in patients with a hypersensitivity to levetiracetam. Reactions have included anaphylaxis and angioedema.

ADVERSE REACTIONS
Most common adverse reactions in adults experiencing partial onset seizures, asthenia, somnolence, and dizziness occurred predominantly during the first 4 weeks of treatment with EMSCOT.
The most common adverse reactions in pediatric patients receiving EMSCOT in combination with other AEDs, are fatigue, aggression, nasal congestion, decreased appetite, and irritability.

DRUG INTERACTIONS
Levetiracetam circulates largely unbound (<10% bound) to plasma proteins; clinically significant interactions with other drugs through competition for protein binding sites are therefore unlikely.
Drug-Drug Interactions Between EMSCOT And Other Antiepileptic Drugs (AEDs)
Phenytoin EMSCOT (3000 mg daily) had no effect on the pharmacokinetic disposition of phenytoin in patients with refractory epilepsy. Pharmacokinetics of levetiracetam were also not affected by phenytoin.
Valproate EMSCOT (1500 mg twice daily) did not alter the pharmacokinetics of valproate in healthy volunteers. Valproate 500 mg twice daily did not modify the rate or extent of levetiracetam absorption or its plasma clearance or urinary excretion.
Potential drug interactions between EMSCOT and other AEDs (carbamazepine, gabapentin, lamotrigine, phenobarbital, phenytoin, primidone and valproate) were also assessed by evaluating the serum concentrations of levetiracetam and these AEDs during placebo-controlled clinical studies. These data indicate that levetiracetam does not influence the plasma concentration of other AEDs and that these AEDs do not influence the pharmacokinetics of levetiracetam.
Other Drug Interactions
Oral Contraceptives EMSCOT do not influence the pharmacokinetics of an oral contraceptive containing 0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel, or of the luteinizing hormone and progesterone levels, indicating that impairment of contraceptive efficacy is unlikely. Coadministration of this oral contraceptive did not influence the pharmacokinetics of levetiracetam.
Digoxin EMSCOT do not influence the pharmacokinetics and pharmacodynamics (ECG) of digoxin given as a 0.25 mg dose every day. Coadministration of digoxin did not influence the pharmacokinetics of levetiracetam.
Warfarin EMSCOT did not influence the pharmacokinetics of R and S warfarin. Prothrombin time was not affected by levetiracetam. Coadministration of warfarin did not affect the pharmacokinetics of levetiracetam.
Probenecid Probenecid, a renal tubular secretion blocking agent, administered at a dose of 500 mg four times a day, did not change the pharmacokinetics of levetiracetam 1000 mg twice daily. Css max of the metabolite, ucb L057, was approximately doubled in the presence of probenecid while the fraction of drug excreted unchanged in the urine remained the same. Renal clearance of ucb L057 in the presence of probenecid decreased 60%, probably related to competitive inhibition of tubular secretion of ucb L057.
USE IN SPECIFIC POPULATION
Pregnancy
Pregnancy Category C
Levetiracetam blood levels may decrease during pregnancy.
Labor and Delivery
The effect of EMSCOT on labor and delivery in humans is unknown.
Nursing Mothers
Levetiracetam is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from EMSCOT, 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 EMSCOT in the adjunctive treatment of partial onset seizures in pediatric patients age 1 month to 16 years old with epilepsy have been established. The dosing recommendation in these pediatric patients varies according to age group and is weight-based.
Geriatric Use
Levetiracetam is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because 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.
Renal Impairment
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.
WARNINGS AND PRECAUTIONS
Behavioral Abnormalities and Psychotic Symptoms
EMSCOT may cause behavioral abnormalities and psychotic symptoms. Patients treated with EMSCOT should be monitored for psychiatric signs and symptoms.
Suicidal Behavior and Ideation
Antiepileptic drugs (AEDs), including EMSCOT, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED 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.
Somnolence and Fatigue
EMSCOT may cause somnolence and fatigue. Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on EMSCOT to gauge whether it adversely affects their ability to drive or operate machinery.
Anaphylaxis and Angioedema
EMSCOT can cause anaphylaxis or angioedema after the first dose or at any time during treatment. Signs and symptoms include hypotension, hives, rash, respiratory distress, and swelling of the face, lip, mouth, eye, tongue, throat, and feet. EMSCOT should be discontinued and the patient should seek immediate medical attention. EMSCOT should be discontinued permanently if a clear alternative etiology for the reaction cannot be established.
Serious Dermatological Reactions
Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), may occur in both pediatric and adult patients treated with EMSCOT. EMSCOT 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 EMSCOT, should be withdrawn gradually to minimize the potential of increased seizure frequency.
Hematologic Abnormalities
EMSCOT can cause hematologic abnormalities. Hematologic abnormalities include decreases in red blood cell (RBC) counts, hemoglobin, and hematocrit, and increases in eosinophil counts.
Seizure Control During Pregnancy
Physiological changes may gradually decrease plasma levels of levetiracetam throughout pregnancy. This decrease is more pronounced during the third trimester. It is recommended that patients be monitored carefully during pregnancy. Close monitoring should continue through the postpartum period especially if the dose was changed during pregnancy.

DOSAGE AND ADMINISTRATION
Dosing for Partial Onset Seizures
Adults 16 Years and Older Initiate treatment with a daily dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Additional dosing increments may be given (1000 mg/day additional every 2 weeks) to a maximum recommended daily dose of 3000 mg. There is no evidence that doses greater than 3000 mg/day confer additional benefit.
Pediatric Patients
- ***1 Month to < 6 Months***
  Initiate treatment with a daily dose of 14 mg/kg in 2 divided doses (7 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 14 mg/kg to the recommended daily dose of 42 mg/kg (21 mg/kg twice daily). In the clinical trial, the mean daily dose was 35 mg/kg in this age group. The effectiveness of lower doses has not been studied.
- **6 Months to < 4 Years:**
  Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose in 2 weeks by an increment of 20 mg/kg to the recommended daily dose of 50 mg/kg (25 mg/kg twice daily). If a patient cannot tolerate a daily dose of 50 mg/kg, the daily dose may be reduced.
- **4 Years to < 16 Years**
  Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 mg/kg twice daily). If a patient cannot tolerate a daily dose of 60 mg/kg, the daily dose may be reduced. In the clinical trial, the mean daily dose was 44 mg/kg. The maximum daily dose was 3000 mg/day.

For EMSCOT tablet dosing in pediatric patients weighing 20 to 40 kg, initiate treatment with a daily dose of 500 mg given as twice daily dosing (250 mg twice daily). Increase the daily dose every 2 weeks by increments of 500 mg to a maximum recommended daily dose of 1500 mg (750 mg twice daily).

For EMSCOT tablet dosing in pediatric patients weighing more than 40 kg, initiate treatment with a daily dose of 1000 mg/day given as twice daily dosing (500 mg twice daily). Increase the daily dose every 2 weeks by increments of 1000 mg/day to a maximum recommended daily dose of 3000 mg (1500 mg twice daily).

Dosing for Myoclonic Seizures in Patients 12 Years of Age and Older with Juvenile Myoclonic Epilepsy:
Initiate treatment with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Increase the dosage by 1000 mg/day every 2 weeks to the recommended daily dose of 3000 mg. The effectiveness of doses lower than 3000 mg/day has not been studied.

Dosing for Primary Generalized Tonic-Clonic Seizures
Adults 16 Years and Older
Initiate treatment with a dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily). Increase dosage by 1000 mg/day every 2 weeks to the recommended daily dose of 3000 mg. The effectiveness of doses lower than 3000 mg/day has not been adequately studied.
Pediatric Patients Ages 6 to < 16 Years
Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 mg/kg twice daily). The effectiveness of doses lower than 60 mg/kg/day has not been adequately studied.

Dosage Adjustments in Adult Patients with Renal Impairment
EMSCOT dosing must be individualized according to the patient's renal function status. Recommended dosage adjustments for adults are shown in Table 1. In order to calculate the dose recommended for patients with renal impairment, creatinine clearance adjusted for body surface area must be calculated. To do this an estimate of the patient's creatinine clearance (CLcr) in mL/min must first be calculated using the following formula:

$$\text{Clcr} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dL)}} \quad (\times 0.85 \text{ for Female Patients})$$

Then CLcr is adjusted for body surface area (BSA) as follows:

$$\frac{\text{Clcr (mL/min/1.73m}^2\text{)} = \text{CLcr (mL/min)}}{\text{BSA subject (m}^2\text{)}} \times 1.73$$

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 500 mg supplemental dose is recommended.

OVERDOSAGE
The highest known dose of EMSCOT received in the clinical development program was 6000 mg/day. Other than drowsiness, there were no adverse reactions.
Management of Overdose
There is no specific antidote for overdose with EMSCOT. 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.
STORAGE/PRECAUTIONS: Store in a cool, dry and dark place between 15- 30 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners.
PRESENTATION: EMSCOT Tablets (250,500 & 750 mg) are available in packing containing 10 film coated tablets.

خوراک: ڈاکٹر کی ہدایت کے مطابق۔

احتیاط: روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ مستند ڈاکٹر کے نسخہ پر فروخت اور استعمال کریں۔

Complete Medical Information available only for doctors on request.

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