Levra
(Levetiracetam) USP

Tablets
Oral Solution
Injection

COMPOSITION
Levra 250mg Tablets:
Each film coated tablet contains:
Levetiracetam (USP).....250mg
Levra 500mg Tablets:
Each film coated tablet contains:
Levetiracetam (USP).....500mg
Levra Oral Solution:
Each 1ml contains:
Levetiracetam (USP).....100mg
Levra IV Injection:
Each 5ml ampoule contains:
Levetiracetam (USP).....500mg

PHARMACOTHERAPEUTIC GROUP
Anti-epileptic

THERAPEUTIC INDICATIONS
LEVRA is indicated as adjunctive therapy in the treatment of partial onset seizures in adults with or without secondary generalization in patients with epilepsy.
Levra is indicated in children 4 years of age and older as adjunctive therapy in the treatment of partial onset seizures with epilepsy. As adjunctive therapy Levra is also indicated in the treatment of myoclonic seizures in adults and adolescents 12 years of age and older with juvenile myoclonic epilepsy. Levra 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.

ADULTS AND ADOLESCENTS OLDER THAN 16 YEARS:
The initial therapeutic dose is 500mg twice daily. This dose can be started on first day of treatment. Depending upon the clinical response and tolerance, the daily dose can be increased upto 1500mg twice daily. Dose changes can be made in 500 mg twice daily increments or decrements every two to four weeks.
ELDERLY: Adjustment of the dose is recommended in elderly patients with compromised renal function.

PATIENTS WITH RENAL IMPAIRMENTS
LEVRA dosing must be individualized according to the patient's renal function status. Recommended doses and adjustment for dose for adults are shown in the Table. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in mL/min is needed. CLcr in mL/min may be estimated from serum creatinine (mg/dL) determination using the following formula:

$$\text{CLcr} = \frac{\text{[140 - age (years)] x weight (kg)}}{\text{72x serum creatinine (mg/dL)}} \quad \text{(x 0.85 for women)}$$

DOSAGE AND ADMINISTRATION

Dosing Schedule for Adult Patients With Impaired Renal Function

Group	Creatinine Clearance (mL/min)	Dosage (mg)	Frequency
Normal	>80	500 to 1,500	Every 12 h
Mild	50-70	500 to 1,000	Every 12 h
Moderate	30-40	250 to 750	Every 12 h
Severe	<30	250 to 500	Every 12 h
ESRD (End Stage Renal Disease) Patients on dialysis	- - -	500 to 1,000	Every 24 h

Partial Onset Seizures (Adults 16 Years and Older)
Treatment should be initiated with a daily dose of 1000mg/day, given as twice-daily dosing (500mg BID). Additional dosing increments may be given (1000mg/day additional every 2 weeks) to a maximum recommended daily dose of 3000mg.
Oral solution dose is between 1000mg (10ml) and 3000mg (30ml) each day. Levra oral solution must be taken twice a day once in the morning and once in the evening.

Pediatric Patients Ages 4 to <16 Years
Treatment should be initiated with a daily dose of 20mg/kg in 2 divided doses (10mg/kg BID). The daily dose should be increased every 2 weeks by increments of 20mg/kg to the recommended daily dose of 60mg/kg (30mg/kg BID). If a patient cannot tolerate a daily dose of 60mg/kg, the daily dose may be reduced. In the clinical trial, the mean daily dose was 52mg/kg. Patients with body weight equals to 20kg should be dosed with oral solution. Patients with body weight above 20kg can be dosed with either tablets or oral solution.

Myoclonic Seizures:
In Patients 12 Years of age and older with Juvenile Myoclonic Epilepsy - Treatment should be initiated with a dose of 1000mg/day, given as twice-daily (500mg BID). Dosage should be increased by 1000mg/day every 2 weeks to the recommended daily dose of 3000mg. The effectiveness of doses lower than 3000mg/day has not been studied.

Primary Generalized Tonic-Clonic Seizures:
Adults 16 Years and Older: Treatment should be initiated with a dose of 1000mg/day, given as twice-daily dosing (500mg BID). Dosage should be increased by 1000mg/day every 2 weeks to the recommended daily dose of 3000mg. The effectiveness of doses lower than 3000mg/day has not been adequately studied.

Pediatric Patients Ages 6 to <16 Years: Treatment should be initiated with a daily dose of 20mg/kg in 2 divided doses (10mg/kg BID). The daily dose should be increased every 2 weeks by increments of 20mg/kg to the recommended daily dose of 60mg/kg (30mg/kg BID). The effectiveness of doses lower than 60mg/kg/day has not been adequately studied.

Replacement Therapy
When switching from oral Levra, the initial total daily intravenous dosage of Levra should be equivalent to the total daily dosage and frequency of oral Levra and should be

administrated as a 15 minute intravenous infusion following dilution in 100ml of a compatible diluent.

Switching to Oral Dosing:
At the end of the intravenous treatment period, the patient may be switched to Levra oral administration at the equivalent daily dosage and frequency of the intravenous administration.

Dosage Schedule:
Levra injection is for intravenous administration only and must be diluted prior to administration. One ampoule of Levra injection contains 500mg Levetiracetam (500mg/5 ml).
To prepare a 1000mg dose dilute 10ml of Levra injection (2 vials of 5ml each) in 100ml of a compatible diluent (0.9% Sodium chloride, Ringer lactate, 5% Dextrose) and administer intravenously as a 15-minute infusion.

PATIENTS WITH HEPATIC IMPAIRMENT
No dose adjustment is needed in patients with mild to moderate Hepatic impairment.

CONTRAINDICATIONS
This product should not be administered to patients who have previously exhibited hypersensitivity to Levetiracetam or any other pyrrolidone derivative.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
In accordance with the current practice if Levra has to be discontinued it is recommended to withdraw it gradually e.g. 500mg twice daily decrements every two to four weeks. An increase in seizure frequency of more than 25% has been reported in 14% and 26% of the Levetiracetam and placebo treated patients, respectively.

Pediatric Patients:
Levra is associated with somnolence, fatigue and behavioral abnormalities.

The administration of Levra to patients with renal impairment may require dose adaptation. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection.

PREGNANCY AND LACTATION
Levetiracetam is pregnancy category C drug. No studies are available on the use of Levra in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for human is unknown. Levra should not be used during pregnancy unless clearly necessary. Discontinuation of anti-epileptic treatments may result in disease worsening, harmful to mother and the fetus.
Levetiracetam is excreted in human breast milk. Therefore breast feeding is not recommended.

UNDESIRABLE EFFECTS
Pooled safety data from clinical studies shows 46.4 % and 42.22% of the patients experienced undesirable effects with Levra use and placebo groups respectively and that 2.4 and 2.2% patients experienced serious undesirable effects in Levra and placebo group respectively. The most common observed side effects were somnolence, asthenia and dizziness. In pooled safety analysis there was no clear dose response relationship but incidence and severity of CNS related side effects decreased over time.

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
Very common: Asthenia

NERVOUS SYSTEM DISORDERS
Very common: Somnolence
Common: Amnesia, ataxia, convulsions, dizziness, headache, tremor, psychiatric disorders.

BLOOD AND LYMPHATIC SYSTEM DISORDERS
Neutropenia, pancytopenia, thrombocytopenia

OVER-DOSE SYMPTOMS
Somnolence, Agitation, Aggression, Depressed level of consciousness, Respiratory depression, Coma

DOSE:
As directed by the physician.

INSTRUCTIONS
Store at 15-30°C. Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
For Tablets: Protect from heat, light and moisture.
For Solution/Injection: Protect from heat and light.

PRESENTATION
Levra 250mg Tablets: Available in blister pack of 3x10's.
Levra 500mg Tablets: Available in blister pack of 1x10's.
Levra Oral Solution: (100mg/ml) 60ml pack.
Levra IV Injection: (500mg/5ml ampoule) Pack of 1's.

اورل سلوشن
گولیاں
انجیکشن

لیورا

(لیویٹانریسیٹیم) یو ایس پی

خوراک: دوا ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: دوا کو **15-30°** سینٹی گریڈ پر رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔
برائے ٹیبلیٹس: گرمی، روشنی اور نمی سے محفوظ رکھیں۔
برائے سلوشن/انجیکشن: گرمی اور روشنی سے محفوظ رکھیں۔

Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD
20 Km Ferozepur Road Lahore, Pakistan.

0603-00