Vlep® 500mg

(Vigabatrin)
Tablets U.S.P.

ویلیپ ۵۰۰ ملی گرام
(ویگابیٹرن) ٹیبلٹس یو۔ایس۔پی۔

QUALITATIVE AND QUANTITATIVE COMPOSITION
Vlep 500mg Tablets U.S.P.:
Each film-coated tablet contains:
Vigabatrin U.S.P. 500mg

DESCRIPTION:
Vlep (vigabatrin) is an oral antiepileptic drug and is available as film-coated 500mg tablet.

CLINICAL PHARMACOLOGY:
Mechanism of Action: The precise mechanism of Vigabatrin's anti-seizure effect is unknown, but it is believed to be the result of its action as an irreversible inhibitor of γ-aminobutyric acid transaminase (GABA-T), the enzyme responsible for the metabolism of the inhibitory neurotransmitter GABA. This action results in increased levels of GABA in the central nervous system. **Pharmacodynamics: Effects on Electrocardiogram :** There is no indication of a QT/QTc prolonging effect of Vigabatrin in single doses up to 6.0g. Peak concentrations for 6.0g. **Pharmacokinetics:** Vigabatrin displayed linear pharmacokinetics after administration of single doses ranging from 0.5g to 4g, and after administration of repeated doses of 0.5g and 2.0g twice daily. **Absorption:** Following oral administration, vigabatrin is essentially completely absorbed. The time to maximum concentration (Tmax) is approximately 1 hour for children (10 years – 16 years) and adults, and approximately 2.5 hours for infants (5 months - 2 years). There was little accumulation with multiple dosing in adult and pediatric patients. A food effect study involving administration of vigabatrin to healthy volunteers under fasting and fed conditions indicated that the Cmax was decreased by 33%, Tmax was increased to 2 hours, and AUC was unchanged under fed conditions. **Distribution:** Vigabatrin does not bind to plasma proteins. Vigabatrin is widely distributed throughout the body; mean steady-state volume of distribution is 1.1 L/kg (CV = 20%). **Metabolism and Elimination:** Vigabatrin is not significantly metabolized; it is eliminated primarily through renal excretion. The terminal half-life of vigabatrin is about 5.7 hours for infants (5 months – 2 years), 9.5 hours for children (10 years – 16 years), and 10.5 hours for adults. Following administration of C-vigabatrin to healthy male volunteers, about 95% of total radioactivity was recovered in the urine over 72 hours with the parent drug representing about 80% of this. Vigabatrin induces CYP2C9, but does not induce other hepatic cytochrome P450 enzyme systems. **Renal Impairment:** Mean AUC increased by 30% and the terminal half-life increased by 55% (8.1 hr vs 12.5 hr) in adult patients with mild renal impairment (CLcr from >50-80 mL/min) in comparison to normal subjects. Mean AUC increased by two-fold and the terminal half-life increased by two-fold in adult patients with moderate renal impairment (CLcr from >30-50 mL/min) in comparison to normal subjects. Mean AUC increased by 4.5-fold and the terminal half-life increased by 3.5-fold in adult patients with severe renal impairment (CLcr from >10-30 mL/min) in compari-son to normal subjects. **Adult patients with renal impairment:** Dosage adjustment, including starting at a lower dose, is recommended for adult patients with any degree of renal impairment.
Infants with renal impairment: Information about how to adjust the dose in infants with renal impairment is unavailable.
Pediatric patients 10 years and older with renal impairment: Although information is unavailable on the effects of renal impairment on vigabatrin clearance in pediatric patients 10 years and older, dosing can be calculated based upon adult data and an established formula. **Hepatic Impairment:** Vigabatrin is not significantly metabolized. The pharmacokinetics of Vigabatrin in patients with impaired liver function has not been studied.

INDICATIONS AND USAGE:
Refractory Complex Partial Seizures (CPS) Vlep is indicated as adjunctive therapy for adults and pediatric patients 10 years of age and older with refractory complex partial seizures. Vlep is not indicated as a first line agent for complex partial seizures.
Infantile Spasms (IS): Vlep is indicated as monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age.

CONTRAINDICATIONS: None

INTERACTIONS: • Phenytoin • Clonazepam • Other AEDs • Alcohol • Oral Contraceptives .
Drug-Laboratory Test Interactions Vlep decreases alanine transaminase (ALT) and aspartate transaminase (AST) plasma activity in up to 90% of patients. Vlep may increase the amount of amino acids in the urine, possibly leading to a false positive test for certain rare genetic metabolic diseases (e.g., alpha aminoadipic aciduria).

USE IN SPECIFIC POPULATION:
Pregnancy: Pregnancy Category C. Vigabatrin produced developmental toxicity, including teratogenic and neurohistopatho-logical effects. Vlep should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Breast feeding: Vigabatrin is excreted in human milk. Because of the potential for serious adverse reactions from Vigabatrin in nursing infants a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE REACTIONS:
The following are the adverse reactions:
Magnetic Resonance Imaging (MRI) abnormalities in

Infants, neurotoxicity, suicidal behavior and Ideation, withdrawal of Antiepileptic Drugs (AEDs), anemia, somnolence and fatigue, peripheral neuropathy, weight gain, edema, birth defects, deafness, delayed puberty, gastrointestinal hemorrhage, esophagitis, developmental delay, facial edema, malignant hyperthermia, multi-organ failure, cholestasis, dystonia, encephalopathy, hypertonia, hypotonia, muscle spasticity, myoclonus, optic neuritis, Acute psychosis, apathy, delirium, hypomania, neonatal agitation, psychotic disorder, Laryngeal edema, pulmonary embolism, respiratory failure, stridor, Angioedema, maculo-papular rash, pruritus, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)

DOSAGE AND ADMINISTRATION: Refractory Complex Partial Seizures Adults (Patients >16 Years of Age): Treatment should be initiated at 1000 mg/day (500 mg twice daily). Total daily dose may be increased in 500 mg increments at weekly intervals depending on response. The recommended dose of Vlep in adults is 3000 mg/day (1500 mg twice daily). **Pediatric Patients 10 to 16 Years of Age:** Treatment should be initiated at a total daily dose of 500 mg/day (250 mg twice daily) and may be increased weekly to a total maintenance dose of 2000mg/day (1000mg twice daily). Patients weighing more than 60 kg should be dosed according to adult recommendations.

Pediatric CPS Dosing Recommendations:

Body Weight [kg]	Total Daily Starting Dose [mg/day]	Total Daily Maintenance Dose [mg/day]
25 to 60	500	2000

Infantile Spasms: The initial daily dosing is 50 mg/kg/day given in two divided doses; subsequent dosing can be titrated by 25 mg/kg/day to 50 mg/kg/day increments every 3 days up to a maximum of 150mg/kg/-day given in 2 divided doses.

Patients with Renal Impairment

Infants: Information about how to adjust the dose in infants with renal impairment is unavailable. Pediatric patients 10 years and older, and adult patients Mild renal impairment (CLcr >50 - 80 mL/min): dose should be decreased by 25% Moderate renal impairment (CLcr >30 - 50 mL/min): dose should be decreased by 50% Severe renal impairment (CLcr >10 - 30 mL/min): dose should be decreased by 75%.

Overdose: Signs, Symptoms, and Laboratory Findings of Overdosage: Coma, unconsciousness, and/or drowsiness are described in the majority of cases of vigabatrin overdose. Other less commonly reported symptoms included vertigo, psychosis, apnea or respiratory depression, bradycardia, agitation, irritability, confusion, headache, hypotension, abnormal behavior, increased seizure activity, status epilepticus, and speech disorder. These symptoms resolved with supportive care. **Management of Overdosage:** There is no specific antidote for Vlep overdose. Standard measures to remove unabsorbed drug should be used, including elimination by emesis or gastric lavage. Supportive measures should be employed, including monitoring of vital signs and observation of the clinical status of the patient.

Missed Dose: Before starting to take Vlep, talk to your healthcare provider about what you or your child should do if a Vlep dose is missed.

INSTRUCTIONS:

Dosage as directed by the physician.
Store below 30°C.
Protect from heat,light and moisture.
Keep all medicines out of the reach of children.

PRESENTATION:

Vlep 500mg Tablets U.S.P.: Available in Alu/Alu Blister of 10's Tablets packed in carton.

علامات/طریقہ استعمال:

ویلپ ٹیبلٹس ۱۰ سال اور اس سے زیادہ عمر کے مریضوں میں پیچیدہ جزوی دوروں کے لئے تجویز کردہ ہے ویلپ ساشے ۱ ماہ سے ۲ سال کی عمر کے بچوں میں اسپاسم کے لئے مونوتھراپی کے طور پر تجویز کردہ ہے۔

عمومی خوراک:

خوراک ڈاکٹر کی ہدایت کے مطابق لیں۔

دوا کھانے کے ساتھ یا بغیر کھانے کے لی جا سکتی ہے۔

مضر اثرات:

نیوروٹوکسسٹی، خودکشی کے خیالات، پیدائشی عیب، وزن کا بڑھاؤ، متعدد اعضاء کی خرابی۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔

روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

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