NERVILIN CAPSULES
Pregabalin 25mg/75mg

Composition:
Each capsule contains:
Pregabalin 25mg.
Pregabalin 75mg
Pharmacology:
Pregabalin is a new anticonvulsant drug indicated as an add on therapy for partial onset seizures and for certain types of neuropathic pain. Pregabalin binds to the alpha2-delta subunit of the voltage-gated calcium channel in the central nervous system. Pregabalin binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues is involved in pregabalin's antinociceptive and antiseizure effects .In vitro, Pregabalin reduces the calcium-dependent release of several neurotransmitters, possibly by modulation of calcium channel function. Although Pregabalin is a structural derivative of inhibitory neurotransmitter gamma-aminobutyric acid (GABA), it does not bind directly to GABA or benzodiazepine receptors.
Pharmacokinetics:
Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentrations occurring within 1 hour following both single and multiple dose administration. Pregabalin oral bioavailability is estimated to be ≥ 90% and is independent of dose. Following repeated administration, steady state is achieved within 24 to 48 hours. The rate of pregabalin absorption is decreased when given with food resulting in a decrease in C_{max} by approximately 25-30% and a delay in t_{max} to approximately 2.5 hours.
In humans, the apparent volume of distribution of pregabalin following oral administration is approximately 0.56 l/kg. Pregabalin is not bound to plasma proteins.
Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabelled pregabalin, approximately 98% of the radioactivity recovered in the urine was unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of the dose.
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Mean elimination half-life is 6.3 hours. Plasma clearance and renal clearance are directly proportional to creatinine clearance. Dose adjustment in patients with reduced renal function or undergoing haemodialysis is necessary.
Pregabalin is effectively removed from plasma by haemodialysis (following a 4 hour haemodialysis treatment plasma pregabalin concentrations are reduced by approximately 50%). Because renal elimination is the major elimination pathway, dose reduction in patients with renal impairment and dose supplementation following haemodialysis is necessary.
Paediatric patients with epilepsy (age groups: 1 to 23 months, 2 to 6 years, 7 to 11 years and 12 to 16 years) at dose levels of 2.5, 5, 10 and 15 mg/kg/day in a pharmacokinetic and tolerability study.
After oral administration of pregabalin in paediatric patients in the fasted state, in general, time to reach peak plasma concentration was similar across the entire age group and occurred 0.5 hours to 2 hours post dose.
Pregabalin Cmax and AUC parameters increased in a linear manner with increasing dose within each age group. The AUC was lower by 30% in paediatric patients below a weight of 30 kg due to an increased body weight adjusted clearance of 43% for these patients in comparison to patients weighing ≥30 kg.
Pregabalin terminal half-life averaged about 3 to 4 hours in paediatric patients up to 6 years of age, and 4 to 6 hours in those 7 years of age and older.
Population pharmacokinetic analysis showed that creatinine clearance was a significant covariate of pregabalin oral clearance, body weight was a significant covariate of pregabalin apparent oral volume of distribution, and these relationships were similar in paediatric and adult patients.
Pregabalin pharmacokinetics in patients younger than 3 months old have not been studied.
In Elderly (over 65 years of age), Pregabalin clearance tends to decrease with increasing age. This decrease in oral clearance is consistent with decreases in creatinine clearance associated with increasing age. Reduction of pregabalin dose may be required in patients who have age related compromised renal function.
The pharmacokinetics of 150 mg pregabalin in breast-feeding mothers given every 12 hours (300 mg daily dose) was evaluated in 10 lactating women who were at least 12 weeks postpartum. Lactation had little to no influence on pregabalin pharmacokinetics. Pregabalin was excreted into breast milk with average steady-state concentrations approximately 76% of those in maternal plasma. The estimated infant dose from breast milk (assuming mean milk consumption of 150 ml/kg/day) of women receiving 300 mg/day or the maximum dose of 600 mg/day would be 0.31 or 0.62 mg/kg/day, respectively. These estimated doses are approximately 7% of the total daily maternal dose on a mg/kg basis.
Indications:
Nervilin is indicated for the treatment of peripheral and central neuropathic pain in adults.
It is also an adjunctive therapy in adults with partial seizures with or without secondary generalization.
Nervilin is also indicated for the treatment of Generalized Anxiety Disorder (GAD) in adults.
Dosage & Administration
Method of administration: Nervilin is for oral use only. It may be taken with or without food.
Posology: The dose range is 150 to 600 mg per day given in either two or three divided doses.
Neuropathic pain: Pregabalin treatment can be started at a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval.
Epilepsy: Pregabalin treatment can be started with a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. The maximum dose of 600 mg per day may be achieved after an additional week.
Generalized Anxiety Disorder: The dose range is 150 to 600 mg per day given as two or three divided doses. The need for treatment should be reassessed regularly. Pregabalin treatment can be started with a dose of 150 mg per day. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. Following an additional week the dose may be increased to 450 mg per day. The maximum dose of 600 mg per day may be achieved after an additional week.
Patients with renal impairment
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. As pregabalin clearance is directly proportional to creatinine clearance, dose reduction in patients with compromised renal function must be individualized according to creatinine clearance (CLcr) as indicated in Table 1 determined using the following formula:

$$CL_{cr}(ml/min) = \left[\frac{1.23 \times [140 - age\,(years)] \times weight\,(kg)}{serum\ creatinine\ (\mu mol\,l)}\right] (\times\ 0.85 \text{ for female patients})$$

Pregabalin is removed effectively from plasma by haemodialysis (50% of drug in 4 hours). For patients receiving haemodialysis, the pregabalin daily dose should be adjusted based on renal function. In addition to the daily dose, a supplementary dose should be given immediately following every 4-hour haemodialysis treatment.
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Patients with hepatic impairment: No dose adjustment is required for patients with hepatic impairment.
Paediatric population: The safety and efficacy of pregabalin in children below the age of 12 years and in adolescents (12-17 years of age) have not been established.
Elderly (over 65 years of age) population: Elderly patients may require a dose reduction of pregabalin due to a decreased renal function.
Contraindications:
Hypersensitivity to the active substance or to any of the excipients used in manufacture of Nervilin
Side Effects:
The most commonly reported adverse reactions were dizziness, somnolence, headache, Nasopharyngitis, Appetite increased, Euphoric mood, confusion, irritability, disorientation, insomnia, libido decreased, Ataxia, coordination abnormal, tremor, dysarthria, amnesia, memory impairment, disturbance in attention, paraesthesia, hypoaesthesia, sedation, balance disorder and lethargy.
Other include: Vertigo, Vomiting, *nausea,* constipation, *diarrhoea,*
flatulence, abdominal distension, dry mouth, Muscle cramp, arthralgia, back pain, pain in limb, cervical spasm Erectile dysfunction, Oedema peripheral, oedema, gait abnormal, fall, feeling drunk, feeling abnormal, fatigue and Weight increased.
Drug interactions:
Since pregabalin is predominantly excreted unchanged in the urine, it undergoes negligible metabolism in humans (< 2% of a dose recovered in urine as metabolites), does not inhibit drug metabolism in vitro, and is not bound to plasma proteins, it is unlikely to produce, or be subject to, pharmacokinetic interactions.
Pregnancy and lactation:
As the potential risk for humans is unknown, effective contraception must be used in women of child bearing potential.
Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.
Nervilin 25 should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus).
Pregabalin is excreted into human milk. The effect of pregabalin on newborns/infants is unknown. A decision must be made whether to discontinue breast-feeding or to discontinue pregabalin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.
In a clinical trial to assess the effect of pregabalin on sperm motility, healthy male subjects were exposed to pregabalin at a dose of 600 mg/day. After 3 months of treatment, there were no effects on sperm motility.
A fertility study in female rats has shown adverse reproductive effects. Fertility studies in male rats have shown adverse reproductive and developmental effects. The clinical relevance of these findings is unknown.
Overdosage:
The most commonly reported adverse reactions observed when pregabalin was taken in overdose included somnolence, confusional state, agitation, and restlessness.
Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary.
Presentation:
Blister pack of 3 x 10`s per unit box.
Storage conditions:
Store in a cool, dry place below 30°C.Protect from direct sun light.
Keep all medicines out of reach of children.
Manufactured By:

DAWA Limited, Plot No. 7879/8, Baba Dogo Road, Ruaraka
P. O. Box 16633 – 00620, Nairobi, Kenya.

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