

Reslorton[®]

(As Per Innovator's Specification)

Pregabalin

(Manufacturer Specification)

50mg, 75mg, 100mg & 150mg Capsules

COMPOSITION

Reslorton 50mg Capsules: Each capsule contains:

Pregabalin 50mg

(As Per Innovator's Specification)

Reslorton 75mg Capsules: Each capsule contains:

Pregabalin 75mg

(As Per Innovator's Specification)

Reslorton 100mg Capsules: Each capsule contains:

Pregabalin 100mg

(As Per Innovator's Specification)

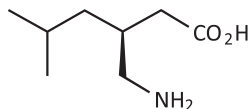
Reslorton 150mg Capsules: Each capsule contains:

Pregabalin 150mg

(As Per Innovator's Specification)

DESCRIPTION

RESLORTON (Pregabalin) is described chemically as (S)-3-(aminomethyl)-5-methylhexanoic acid and molecular formula is $C_9H_{17}NO_2$, and the structural formula is:



CLINICAL PARTICULARS

Therapeutic Indications:

RESLORTON (Pregabalin) is indicated for the following:

- Management of neuropathic pain associated with diabetic peripheral neuropathy.
- Management of postherpetic neuralgia.
- Adjunctive therapy for adult patient with partial onset seizures.
- Management of fibromyalgia.

Dosage and administration

RESLORTON (Pregabalin) is given orally with or without food. When discontinuing **RESLORTON** (Pregabalin), taper gradually over a minimum of 1 week irrespective of indication.

Neuropathic pain associated with diabetic peripheral neuropathy:

RESLORTON (Pregabalin) treatment can be started at a dose of 150 mg per day, given as 2-3 divided doses. Based on individual patient response and tolerability, the dose can be increased to 300 mg, given as 2 divided doses, after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7 days interval.

Post herpetic neuralgia: The recommended dose of **RESLORTON** (Pregabalin) is 75 to 150 mg two times a day, or 50 to 100 mg three times a day (150 to 300 mg/day). The dose may be increased to 300 mg/day within 1 week based on efficacy and tolerability. Because **RESLORTON** (Pregabalin) is eliminated primarily by renal excretion adjust the dose in patient with reduced renal function. Patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300 mg/day, and who are able to tolerate **RESLORTON** (Pregabalin), may be treated with up to 300 mg two times a day, or 200 mg three times a day (600mg/day).

Adjunctive therapy for adult patients with partial onset seizures:

RESLORTON (Pregabalin) at doses of 150 to 600 mg/day has been shown to be effective as adjunctive therapy in the treatment of partial onset seizures in adults. Both the efficacy and adverse event profile of **RESLORTON** (Pregabalin) have been shown to be dose-related. Administer the total daily dose in two or three divided doses. In general, it is recommended that patients be started on a total daily dose no greater than 150 mg/day (75 mg two times a day, or 50 mg three times a day). Based on individual patient response and tolerability, the dose may be increased to a maximum dose of 600 mg/day. Because **RESLORTON** (Pregabalin) is eliminated primarily by renal excretion; adjust the dose in patients with reduced renal function.

Management of Fibromyalgia: The recommended dose of

RESLORTON (Pregabalin) for fibromyalgia is 300 to 450 mg/day. Begin dosing at 75 mg two times a day (150 mg/day). The dose may be increased to 150 mg two times a day (300 mg/day) within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg two times a day (450 mg/day). Although **RESLORTON** (Pregabalin) was also studied at 600 mg/day, there is no evidence that this dose confers additional benefit and this dose was less well

tolerated. In view of the dose-dependent adverse reactions, treatment with doses above 450 mg/day is not recommended.

Contraindications

RESLORTON (Pregabalin) is contraindicated in patients with known hypersensitivity to Pregabalin or any of its components. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **RESLORTON** (Pregabalin).

Precautions

Angioedema: Angioedema may occur in patient during initial and chronic treatment with **RESLORTON** (Pregabalin). Specific symptoms included swelling of the face, mouth (tongue, lips and gums) and neck (throat and larynx). Discontinue **RESLORTON** (Pregabalin) immediately in patients with these symptoms. Exercise caution when prescribing **RESLORTON** (Pregabalin) to patients who have had a previous episode of angioedema. In addition, patient who are taking other drugs associated with angioedema (e.g., angiotensin converting enzyme inhibitors (ACE-inhibitors)) may be at increased risk of developing angioedema.

Withdrawal of Antiepileptic Drugs (AEDs): As with all AEDs, withdrawal

RESLORTON (Pregabalin) gradually to minimize the potential of increased seizure frequency in patients with seizures disorders. If **RESLORTON** (Pregabalin) is discontinued this should be done gradually over a minimum of 1 week.

Suicidal Behavior and Ideation: Antiepileptic drugs (AEDs); including **RESLORTON** (Pregabalin), increase the risk of suicidal thoughts or behaviors in patients taking these drugs for any indication. Monitor patients treated with any AED for any indication for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Dizziness or Somnolence: **RESLORTON** (Pregabalin) may cause dizziness or somnolence. Inform patients that Pregabalin-related dizziness and somnolence may impair their ability to perform tasks such as driving or operating machinery.

Weight Gain: **RESLORTON** (Pregabalin) treatment may cause weight gain. **RESLORTON** (Pregabalin) associated weight gain is related to dose and duration of exposure.

Abrupt or Rapid Discontinuation: Following abrupt or rapid discontinuation of **RESLORTON** (Pregabalin), some patients may have symptoms including insomnia, nausea, headache and diarrhea. Taper **RESLORTON** (Pregabalin) gradually over a minimum of 1 week rather than discontinuing the drug abruptly.

Creatine Kinase Elevation: **RESLORTON** (Pregabalin) treatment is associated with creatine kinase elevations. Instruct patients to promptly report unexplained muscle pain, tenderness, or weakness, particularly if these muscle symptoms are accompanied by malaise or fever. Discontinue treatment with **RESLORTON** (Pregabalin) if myopathy is diagnosed or suspected or if markedly elevated creatine kinase levels occur.

Drug interactions

Since **RESLORTON** (Pregabalin) is predominantly excreted unchanged in the urine, it undergoes negligible metabolism in humans (<2% of a dose recovered in urine as metabolites), and does not bind to plasma proteins, therefore its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions or protein binding displacement. Specifically, there are no pharmacokinetic interactions between **RESLORTON** (Pregabalin) and the following antiepileptic drugs: carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital, and topiramate. Important pharmacokinetic interactions would also not be expected to occur between **RESLORTON** (Pregabalin) and commonly used antiepileptic drugs. Although no pharmacokinetic interactions are seen, additive effects on cognitive and gross motor functioning were seen when **RESLORTON** (Pregabalin) was co-administered with oxycodone, lorazepam or ethanol these drugs.

Pregnancy

Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Use **RESLORTON** (Pregabalin) during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Nursing Mother: It is not known that **RESLORTON** (Pregabalin) is excreted in human milk. It is important to decide whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric use

The safety and efficacy of **RESLORTON** (Pregabalin) in pediatric patients have not been established.

Geriatric use

RESLORTON (Pregabalin) oral clearance tended to decreased with increasing age. This decrease in **RESLORTON** (Pregabalin) oral clearance is consistent with age-related decreases in CL_{CR}. Reduction of **RESLORTON** (Pregabalin) dose may be required in patients who have age-related compromised renal function.

Adverse reactions

Adverse effects that are most common with **RESLORTON** (Pregabalin) treatment include dizziness, somnolence, ataxia, confusion, and asthenia, and blurred vision, difficulty in concentration, incoordination and peripheral edema.

Other adverse events that are reported with **RESLORTON** (Pregabalin) treatment include the following:

Ear and Labyrinth Disorders: Vertigo

Gastrointestinal Disorder: Dry mouth, Constipation, vomiting, Flatulence, Abdominal distension

General Disorders and Administrative Site Conditions: Fatigue, Edema peripheral, Chest pain, Feeling abnormal, Edema, Feeling drunk

Infections and Infestations: Sinusitis

Investigations: Weight Increased

Metabolism and Nutrition Disorders: Increased appetite, Fluid retention,

Musculoskeletal and Connective Tissue Disorders: Arthralgia, Muscle spasms, Back pain

Psychiatric Disorders: Euphoric Mood, Confusion state, Anxiety, Disorientation

CLINICAL PHARMACOLOGY

Mechanism of action:

Pregabalin binds with high affinity to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues. Although the mechanism of action of Pregabalin has not been elucidated, results with genetically modified mice and with compounds structurally related to Pregabalin (such as gabapentin) suggest that binding to the alpha2-delta subunit may be involved in Pregabalin's antinociceptive and anti-seizure effects in animals. In animal models of nerve damage, Pregabalin has been shown to reduce calcium-dependent release of pro-nociceptive neurotransmitter in the spinal cord, possibly by disrupting alpha2-delta containing-calcium channel trafficking and/or reducing calcium currents. Evidence from other animal models of nerve damage and persistent pain suggest that anti-nociceptive activities of Pregabalin may also be mediated through interactions with descending noradrenergic and serotonergic pathways originating from the brainstem that modulate pain transmission in the spinal cord. While Pregabalin is a structural derivative of the inhibitory neurotransmitter gamma amino-butyric acid (GABA), it does not bind directly with GABAA, GABAB, or benzodiazepine receptors does not augment GABAA responses in cultured neurons, does not alter rat brain GABA concentration or have acute effects on GABA uptake or degradation. However, in cultured neurons prolonged application of Pregabalin increases the density of GABA transporter protein and increase the rate of functional GABA transport. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline reuptake.

Pharmacokinetics

Absorption: Following oral administration of Pregabalin capsule under fasting condition, peak plasma concentration occur within 1.5 hours. Pregabalin oral bioavailability is $\geq 90\%$ and is independent of dose. Following single- (25 to 300 mg) and multiple- dose (75 to 900 mg/day) administration, maximum plasma concentrations (C_{max}) and area under the plasma concentration-time curve (AUC) values increase linearly. Following repeated administration, steady state is achieved within 24 to 48 hours. The rate of Pregabalin absorption is decreased when given with the food, resulting in a decrease in C_{max} of approximately 25% to 30% and increase in T_{max} to approximately 3 hours. However, administration of Pregabalin with food has no clinically relevant effect on the total absorption of Pregabalin. Therefore, Pregabalin can be taken with or without food.

Distribution: Pregabalin does not bind to plasma proteins. The apparent volume of distribution of Pregabalin following oral administration is approximately 0.5 L/kg. Pregabalin is a substrate for system L transporter which is responsible for the transport of large amino acids across the blood brain barrier. Although there are no data in humans, Pregabalin has been shown to cross the

blood brain barrier in mice, rat and monkeys. In addition, pregabalin has been shown to cross the placenta in rats and is present in the milk of lactating rats.

Metabolism: Pregabalin undergoes negligible metabolism in humans.

Elimination: Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half-life of 6.3 hours in subjects with normal renal function. Because Pregabalin is not bound to plasma proteins this clearance rate indicates that renal tubular reabsorption is involved. Pregabalin elimination in nearly proportional to creatinine clearance (CL_{Cr}).

SPECIAL POPULATIONS

Renal Insufficiency: **RESLORTON** (Pregabalin) clearance is nearly proportional to creatinine clearance (CL_{Cr}). Dosage reduction in patients with renal dysfunction is necessary. **RESLORTON** (Pregabalin) is effectively removed from plasma by hemodialysis. Following a 4-hours hemodialysis treatment, plasma **RESLORTON** (Pregabalin) concentrations are reduced by approximately 50%. For patients on hemodialysis, dosing must be modified.

OVERDOSAGE

There is no specific antidote for overdose with **RESLORTON** (Pregabalin). If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; observe usual precautions to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient.

STORAGE

Store below 30°C. Protect from light and moisture.

HOW SUPPLIED

RESLORTON 50mg Capsules: Pack of 14 Capsules.

RESLORTON 75mg Capsules: Pack of 14 Capsules.

RESLORTON 100mg Capsules: Pack of 14 Capsules.

RESLORTON 150mg Capsules: Pack of 14 Capsules.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Contains Lactose But Gluten Free

ریسلورٹن
(پری گابالین)

50 ملی گرام، 75 ملی گرام،

100 ملی گرام اور 150 ملی گرام

کپسولز

خوراک و ہدایات

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 30°C سے کم درجہ حرارت پر، نمی اور روشنی سے محفوظ رکھیں۔

INEXT
PHARMACEUTICAL

Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
Plot no. 44-A&B, Sunder Industrial Estate Lahore-Pakistan