

# LAREGAB<sup>TM</sup>- NT

Gabapentin 400 mg and Nortriptyline 10 mg Tablets



## Description:

Laregab-NT is a combination of gabapentin (400 mg) with nortriptyline (10 mg) available as a tablet form. Gabapentin, a medication originally developed for the treatment of epilepsy, presently, gabapentin is widely used to relieve pain, especially neuropathic pain. The molecular formula of gabapentin is  $C_9H_{17}NO_2$  and the molecular weight is 171.24. Nortriptyline is a second-generation tricyclic antidepressant (TCA). It works by increasing the amounts of certain natural substances in the brain that are needed to maintain mental balance.

## Mechanism of Action:

**Gabapentin:** The precise mechanisms by which gabapentin produces its analgesic and antiepileptic actions are unknown. Gabapentin is structurally related to the neurotransmitter gamma-aminobutyric acid (GABA) but has no effect on GABA binding, uptake, or degradation. In vitro studies have shown that gabapentin binds with high-affinity to the  $\alpha 2\delta$  subunit of voltage-activated calcium channels; however, the relationship of this binding to the therapeutic effects of gabapentin is unknown.

**Nortriptyline** is 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten- 5-ylidene)-N-methyl-, hydrochloride with molecular formula  $C_{19}H_{21}N \cdot HCl$  with molecular weight 299.84. Nortriptyline is a metabolite of amitriptyline and it inhibits the reuptake of the biogenic amines, mostly norepinephrine (NE), as well as serotonin (5HT) affect pain transmission in the spinal cord by inhibiting the reuptake of norepinephrine and serotonin, both of which influence descending pain pathways.

## Indication:

-For the management of neuropathic pain

## Dosage:

**Neuropathic Pain –**

As prescribed by the Registered Medical Practitioner.

**Storage:** Store protected from light and moisture at a temperature not exceeding 30°C.

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Gabapentin 400 mg and Nortriptyline 10 mg Tablets

La Renon<sup>®</sup>



# Background:

Pain is an unpleasant sensation and emotion. In the classification of chronic pain, 'NP' is defined as "pain initiated or caused by a primary lesion, dysfunction or transitory perturbation of the peripheral or central nervous system (CNS)". International association for study of pain (IASP) has recently published a new definition of NP, which is defined as "pain caused by a lesion or disease of the somatosensory system"

Neuropathic pain (NP) develops as a consequence of a lesion or disease affecting the somatosensory pathways in the peripheral or central nervous system, and occurs in many neurological diseases (eg, peripheral neuropathy, radiculopathy, spinal cord injury, stroke and multiple sclerosis).

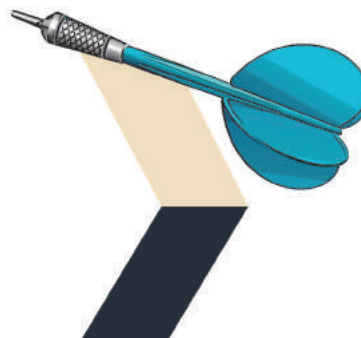
A peculiar feature of NP is the coexistence of negative and positive symptoms and signs, reflecting loss-of-function and gain-of-function of the somatosensory system, respectively.

## How Common is Neuropathic Pain ?

- General population studies, around 7–8% of adults currently have chronic pain with neuropathic characteristics.<sup>1</sup>
- 371 million people diagnosed with diabetes mellitus worldwide and a prevalence of 8.3% as per the Diabetes Atlas2012, diabetes mellitus and approximately 40–50% of the patients developing DPN (Diabetic Peripheral Neuropathy) further develop painful DPN.<sup>2</sup>
- Approximately 20% (18.7–21.4%) of people with cancer have cancer-related neuropathic pain, as a result of either the disease or its treatment.<sup>1</sup>
- 33 million people infected with HIV across the world, around 35% have neuropathic pain, which does not respond well to standard treatments.<sup>1</sup>
- In the India, studies in 2,006 patients with diabetes, 29.2% (586) of people with diabetes were found to have DPN<sup>2</sup>.
- The lifetime incidence of herpes zoster (shingles) is around 25%. Studies in the United States and the Netherlands found that 2.6% and 10%, respectively, will develop chronic postherpetic neuralgia.<sup>1</sup>

## References:

1. International Association for the Study of Pain; 2014-2015 available at <http://iasp.files.cms-plus.com/AM/Images/GYAP/Epidemiology%20of%20Neuropathic%20Pain.pdf>
2. Diabetes Invest; 5: 714–721: 2014



## Clinical Effectiveness:



### 1. Clinical Effectiveness of Gabapentine in Diabetic Peripheral Neuropathy:

*Canadian Agency for Drugs and Technologies in Health; 2015:*

Pooled analysis of clinical efficacy and safety of gabapentin compared with placebo in a subset of adults with diabetic peripheral neuropathy (DPN):

Outcome	No. of RCTs	No. of patients	Patients with benefit (%) G vs plb	RR (95% CI)	NNT (95% CI)
Substantial benefit (≥50% pain reduction or PGIC very much improved)	6	1277	38 vs 21	1.9 (1.5 to 2.3)	5.9 (4.6 to 8.3)
PGIC very much improved	2	408	24 vs 14	1.9 (1.3 to 3.0)	9.6 (5.5 to 35)
Moderate benefit (≥30% pain reduction or PGIC much or very much improved)	7	1439	52 vs 37	1.4 (1.3 to 1.6)	6.6 (4.9 to 9.9)
PGIC much or very much improved	5	695	50 vs 30	1.7 (1.4 to 2.0)	4.9 (3.6 to 7.6)

CI = confidence interval, DPN = diabetic peripheral neuropathy, G = gabapentin, NNT = number needed to treat to benefit, PGIC = Patient Global Impression of Change, plb = placebo, RCT = randomized controlled trial, RR = risk ratio, vs = versus

**Conclusion:** For DPN, gabapentin at dose range of 1200 to 3600 mg is more effective than placebo as assessed by pain measures, such as ≥ 50% reduction in pain, PGIC (much or very much improved). The RR (95% CI) values indicate statistically significant benefit with gabapentin compared with placebo.

### 2. Clinical Effectiveness of Nortriptyline and Gabapentin Combination:

As per *Lancet; 2009:*

- A study on 45 patients with diabetic polyneuropathy or postherpetic neuralgia treated with oral gabapentin, nortriptyline, and combination gabapentin, nortriptyline.
- The patients were randomized (double-blind) in a 1:1:1 ratio and provided treatment as group A (gabapentin 400 mg), Group B (nortriptyline 10 mg), and group C (combination of gabapentin 400 mg & nortriptyline 10 mg), respectively.

#### Results:

- At maximum tolerated dose, Mean daily pain (0–10; numerical rating scale) score was 3.2 (2.5 to 3.8) for gabapentin, 2.9 (2.4 to 3.4) for nortriptyline, and 2.3 (1.8 to 2.8) for combination treatment.

#### Conclusion:

- Combination of gabapentin with nortriptyline is more efficacious than gabapentin or nortriptyline alone for patients who have a partial response to either drug alone and seek additional pain relief.