

Summary of Product Characteristics.

1 Product Name

Pregabalin, Methylcobalamin, Alpha Lipoic acid & Pyridoxine Hydrochloride Capsules (Larykul Plus)

2 Composition

Each hard gelatin capsule contains:

Pregabalin BP.....75mg
Methylcobalamin JP.....750mcg
Alpha Lipoic acid USP.....100mg
Pyridoxine Hydrochloride BP.....3mg
Approved Colours used for capsule shells.

3 Pharmaceutical Form

Hard gelatin Capsule size

4.1 Therapeutic indications

Neuropathic pain

Larykul plus is indicated for the treatment of peripheral and central neuropathic pain in adults.

Epilepsy

Larykul plus is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation.

Generalised Anxiety Disorder

Larykul plus is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.

Fibromyalgia

Larykul Plus is indicated for muscle pain and tenderness.

4.2 Posology and method of administration

Posology

Neuropathic pain

Treatment can be started at a dose of one capsule two or three times a day. Based on individual patient response and tolerability, based on individual patient requirements and tolerance dose should not exceed 3 capsules three times daily.

Epilepsy

Treatment can be started with a dose of one capsule two times a day. Based on individual patient response and tolerability, the dose may be increased to one capsule 3 times a day after 1 week. The maximum dose should not exceed 3 capsules three times daily

Generalised Anxiety Disorder

The dose range is one to three capsules 2 to three times a day. The need for treatment should be reassessed regularly.

Fibromyalgia

Treatment can be started at a dose of one capsule two or three times a day. Based on individual patient response and tolerability, based on individual patient requirements and tolerance dose should not exceed 3 capsules three times daily.

Discontinuation of Pregabalin

In accordance with current clinical practice, if Pregabalin has to be discontinued, it is recommended this should be done gradually over a minimum of 1 week independent of the indication.

Renal impairment

Appropriate corrections to be given in dosage with patients having renal impairment as Pregabalin and its formulations are directly excreted through kidney.

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

Elderly patients may require a dose reduction of Pregabalin due to a decreased renal function

Method of administration

Larykul plus may be taken with or without food.

Larykul Plus is for oral use only.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients.

Patients should discontinue use at least 2 weeks before scheduled surgical procedures.

4.4 Special warnings and precautions for use

Inform your doctor about your current list of medications, over the counter products (e.g. Vitamins, herbal supplements etc) allergies, pre-existing diseases and current health conditions (e.g. Pregnancy, upcoming surgery).

Take as directed by your doctor or follow the direction printed on the product insert.

4.5 Interaction with other medicinal products and other forms of interaction

- Excessive alcohol consumption, antibiotics, anti-acne drugs, anti-retrovirals, anti-gout drugs, anti-hypertensives, anti-tuberculosis drugs, anti-ulcer drugs, biguanides (oral anti-diabetic drugs), histamine (H₂) blocking drugs, oral contraceptives, p[rotein pump inhibitors, sulphonamides (anti-infective), Tetracyclines (anti-infective) and epilepsy (seizure) medication can deplete vitamin B12 levels.
- Thiamine is inactivated by 5-fluorouracil as the latter competitively inhibits the phosphorylation of thiamine to thiamine pyrophosphate.

- Loop diuretics, e.g. furosemide that inhibit tubular reabsorption may cause increased excretion of thiamine in long-term therapy and thus lowering of the thiamine level.
- If taken, simultaneously with L-dopa, vitamin B6 can lessen the dopa effect.
- The simultaneous administration of pyridoxine antagonists (e.g. isoniazide (INH), hydralazine, D-Penicillamine or cycloserine) may increase the vitamin B6 requirement.
- Beverages containing sulphite (e.g. wine) enhance thiamine degradation.
- Since Pregabalin is predominantly excreted unchanged in the urine, 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 likely to produce, or be subject to pharmacokinetic interactions.

4.6 Pregnancy and lactation

There are no adequate data from the use of Larykul plus in pregnant women.

4.7 Effects on ability to drive and use machines

Pregabalin may have minor or moderate influence on the ability to drive and use machines. Pregabalin may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether this medicinal product affects their ability to perform these activities.

4.8 Undesirable effects

- Nausea or stomach upset, along with over-stimulation, fatigue and insomnia.
- Dizziness , Drowsiness, Dry mouth, constipation

4.9 Overdose

The most commonly reported adverse reactions observed when Pregabalin, Methylcobalamin, Pyridoxine was taken in overdose included somnolence, confusional state, agitation and restlessness due to Pregabalin.

5. Pharmacological properties

5.1 Pharmacodynamic properties

- **Methylcobalamin** is the neurologically active form of vitamin B12 and occurs as a water soluble vitamin in the body. It is a cofactor in the enzyme methionine synthase, which functions to transfer methyl groups for the regeneration of methionine from homocysteine. In anaemia, it increases erythrocyte production by promoting nucleic acid synthesis in the bone marrow and by promoting maturation and division of erythrocytes. It is needed for nerve cells and red blood cells and to make DNA. Vitamin B12 deficiency is the cause of several forms of anaemia.

- **Alpha lipoic acid** has enzymatic and cytoprotective effect. It has key role in citric acid cycle, as a coenzyme. Therapeutic efficacy of alpha lipoic acid in diabetic neuropathy is based on reaction with free radicals and lipophylicantioxydants properties.is readily absorbed from the diet or as a supplement. It can regenerate vitamin C from its oxidized form, dehydroascorbic acid, and regenerate other antioxidants. Chelates transition metal ions (e.g. iron and copper), It can enhance the synthesis of glutathione, the main antioxidant within our cells. Glutathione effectively mops up all types of toxins and free radicals. However, we cannot take supplements of this antioxidant since it is unable to cross cell membranes. It can even pitch in and help when the body is lacking vitamin E. When laboratory animals were depleted of their vitamin E stores because their diet lacked this nutrient, they displayed obvious symptoms of vitamin E deficiency. However, when their diet was supplemented with ALA, the animals were completely protected.
- **Pyridoxine Hydrochloride (Vitamin B₆)** is a constituent of the co-enzymes, pyridoxal Pyrophosphate and pyridoxamine phosphate, both of which play an important role in protein metabolism.
- **Pregabalin** binds to an auxiliary subunit { $\alpha 2$ - δ protein} of voltage-gated calcium channels in the central nervous system, hence used for the treatment of peripheral and central neuropathic in adults.

5.2 Pharmacokinetic properties

- **Methylcobalamin** is a water soluble vitamin. It is absorbed in the stomach by proteolysis with the help of Intrinsic factor and is absorbed by active carrier transport mechanism. The Intrinsic Factor B12 complex is absorbed in the terminal ileum. It is stored in the liver. It undergoes enterohepatic circulation and is excreted in small quantities in the urine.
- **Alpha Lipoic Acid** Exogenous racemic alpha lipoic acid orally administered is readily and nearly completely absorbed. Urinary excretion does not play a significant role in its elimination. Therefore, biliary excretion, further electrochemically inactive degradation products, and complete utilization of alpha lipoic acid as a primary substrate in the endogenous metabolism should be considered.
- **Pyridoxine Hydrochloride** is absorbed from the GI tract and is converted to the active form of pyridoxal phosphate. It is excreted in the urine as 4-pyridoxic acid.
- **Pregabalin** is rapidly absorbed when administered in the fasted state, Pregabalin oral bioavailability is estimated to be $\geq 90\%$ and is independent of dose. In preclinical studies, Pregabalin has been shown to cross the blood brain barrier in mice, rats and monkeys. Pregabalin is not bound to plasma proteins. Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug.

5.3 Preclinical safety data

Not available

6. Pharmaceutical particulars

6.1 List of Excipients

Hypromellose 5CPS, Ethylcellulose 20CPS, Polyethylene Glycol 400, Isopropyl alcohol, Dichloromethane, Dibasic calcium phosphate, Micro crystalline cellulose, Croscarmellose sodium, Purified Talc, Sodium lauryl sulfate, Colloidal anhydrous silica, Magnesium stearate.

6.2 Incompatibilities

No major incompatibilities are known.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in a cool and dry place below 30° C. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

ALU/ALU Blister of 10 capsules, such 3 blisters are packed in monocarton along with pack insert.

6.6 Special precautions for disposal and other handling

No special requirement.

7 Marketed in Nigeria by

Geneith Pharm. Limited

12 Adewale Crescent,

Off Oshodi-Apapa Exp. Way

Oshodi, Lagos-Nigeria

8 Manufactured By,

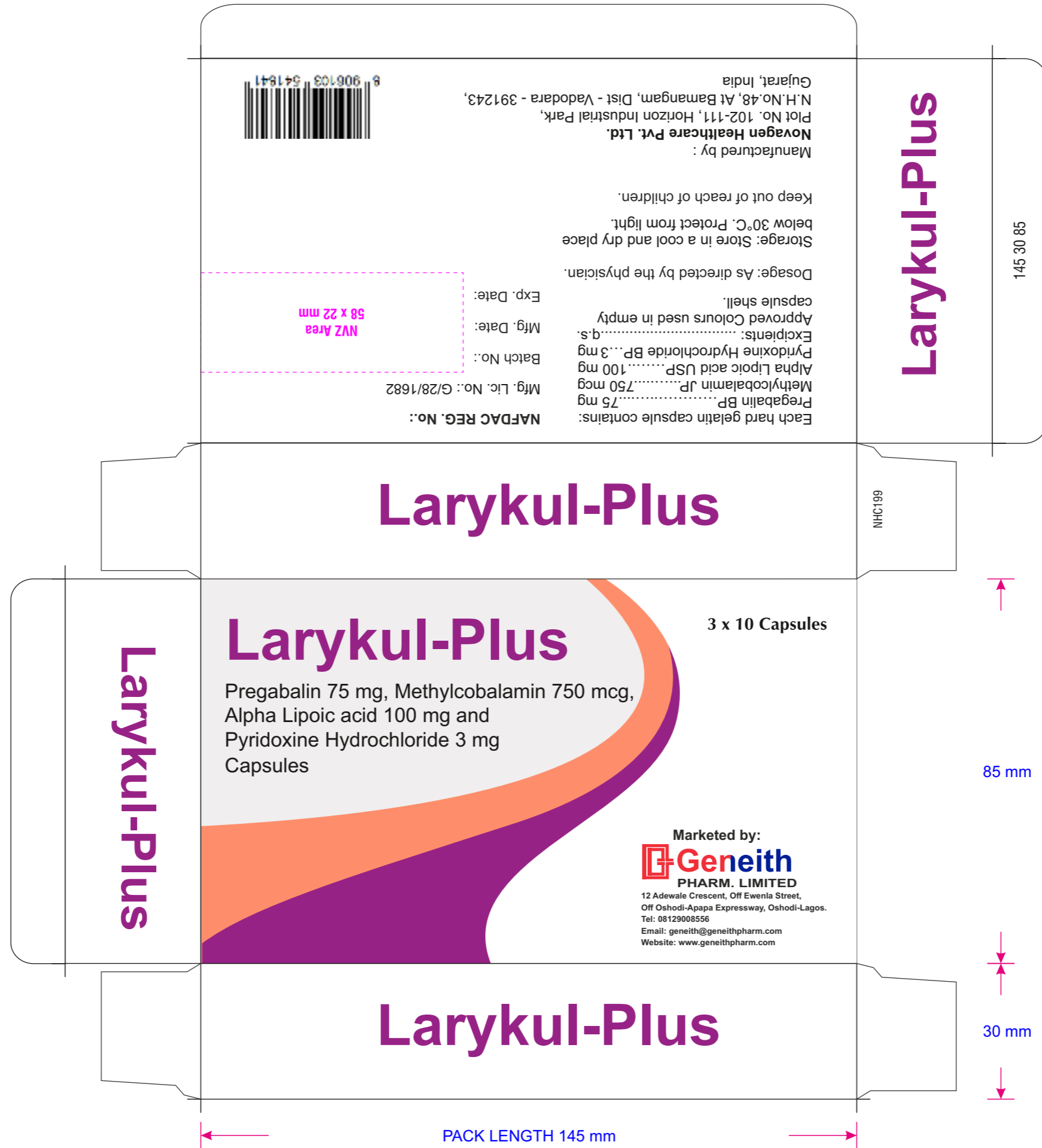
Novagen Healthcare Pvt. Ltd

Plot 102-111, Horizon Industrial Park,

N.H.NO.48, At Bamangam,

Dist-Vadodara-391 243

Gujarat, India



Manufactured by :
Novagen Healthcare Pvt. Ltd.
 Plot No. 102-111, Horizon Industrial Park,
 N.H.No.48, At Bamangam, Dist - Vadodara - 391243,
 Gujarat, India

Keep out of reach of children.
 Storage: Store in a cool and dry place
 below 30°C. Protect from light.
 Dosage: As directed by the physician.

NVZ Area
 58 x 22 mm

NAFDAC REG. No.: G/28/1682
 Mfg. Lic. No.: G/28/1682
 Batch No.:
 Mfg. Date:
 Exp. Date:
 Each hard gelatin capsule contains:
 Pregabalin BP.....75 mg
 Methylcobalamin JF.....750 mcg
 Alpha Lipoic acid USP.....100 mg
 Pyridoxine Hydrochloride BP.....3 mg
 Excipients:q.s.
 Approved Colours used in empty
 capsule shell.

Larykul-Plus

NHC199

Larykul-Plus

3 x 10 Capsules

Pregabalin 75 mg, Methylcobalamin 750 mcg,
 Alpha Lipoic acid 100 mg and
 Pyridoxine Hydrochloride 3 mg
 Capsules

Marketed by:
Geneith
 PHARM. LIMITED
 12 Adewale Crescent, Off Ewenla Street,
 Off Oshodi-Apapa Expressway, Oshodi-Lagos.
 Tel: 08129008556
 Email: geneith@geneithpharm.com
 Website: www.geneithpharm.com

Larykul-Plus

Larykul-Plus

PACK LENGTH 145 mm

145 30 85

85 mm

30 mm