Summary of Product Information

1. Name of the medicinal product

Larykul Forte (Pregabalin, Methylcobalamin, Alpha Lipoic Acid, Pyridoxine HCl & Folic Acid Capsules)

2. Composition

Pregabalin…….....75 mg
Methylcobalamin USP…….750 mcg
Alpha Lipoic Acid USP……100 mg
Pyridoxine Hydrochloride USP…3 mg
Folic Acid USP…….1.5 mg
Excipients……..q.s
Approved colour used in empty capsule shells.

3. Pharmaceutical form

Hard Gelatin Capsule.

4. Clinical particulars

4.1 Therapeutic indications

Larykul Forte is indicated for the treatment of Neuropathic pain, Adjunct in partial seizures, Fibromyalgia, Anxiety.

4.2 Posology and method of administration

Oral

Adult: Initially, 150 mg/day, may increase in increments of 150 mg wkly. Max: 600 mg/day. All
doses to be given in 2 or 3 divided doses.

Renal impairment: Haemodialysis: 25-100 mg immediately after each 4-hr haemodialysis session.

CrCl (ml/min)	**Dosage Recommendation**
30 to <	75 mg/day. Max: 300 mg/day. All doses to be given in 2 or 3

60	divided doses.
15 to < 30	Initially, 25-50 mg/day. Max: 150 mg/day. All doses to be given as a single dose or in 2 divided doses.
<15	Initially, 25 mg/day. Max: 75 mg/day. All doses to be given as a single dose.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients.
- Chronic conditions such as diabetes, thyroid dysfunction may be affected by alpha-lipoic acid supplementation. Please monitor such individuals closely if supplementation is needed. Also, lipoic acid may affect blood glucose control procedures during and after surgery. Patients should discontinue use at least 2 weeks before scheduled surgical procedures.

4.4 Special warnings and precautions for use

- Chronic conditions such as diabetes, thyroid dysfunction may be affected by alpha-lipoic acid. Please monitor such individuals closely if supplementation is needed.
- Protect medicines from moisture & light. keep all medicines out of reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

- Excessive alcohol consumption, antibiotics, anti-acne drugs, anti-retroviral, anti-gout drugs, anti-hypertensive, anti-tuberculosis drugs, anti-ulcer drugs, biguanides (oral anti-diabetic drugs), histamine (H2) blocking drugs, oral contraceptives, proton pump inhibitors, sulfonamides (anti-infectives), tetracyclines(anti-infectives) and epilepsy (seizure) medications 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.

• Alpha-lipoic acid may have additive affects when administered with anti-diabetic drugs. Alpha-lipoic acid may also increase the efficiency of chemotherapeutic drugs.
• 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 unlikely to produce, or be subject to, pharmacokinetic interactions.

4.6 Pregnancy and lactation

Category C: Either studies in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the foetus.

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

1)Nausea or stomach upset, along with over-stimulation, fatigue, and insomnia.
2)High doses of alpha lipoic acid could also potentially lower blood sugar. This is often beneficial to patients who have diabetes, but it requires close monitoring of blood sugar levels. Dizziness, Drowsiness, Dry mouth, Constipation.

4.9 Overdose

Symptoms: Somnolence, agitation, restlessness, confusional state or coma. Management: Symptomatic and supportive treatment. May be removed by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pregabalin

Pregabalin binds to an auxiliary subunit (α2-δ protein) of voltage-gated calcium channels in the central nervous system, hence used for the treatment of peripheral and central neuropathic pain in adults.

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 anemia.

Alpha Lipoic acid

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.

Folic acid

vital for the biosynthesis of purines and thymidylate of nucleic acids. Defective purine biosynthesis due to folate deficiency leads to megaloblastic anemia and macrocytic anemia.

Pyridoxine hydrochloride (Vitamin B_6)

Vitamin B_6 is a constituent of the co-enzymes, pyridoxal pyrophosphate and pyridoxamine phosphate, both of which play an important role in protein metabolism.

5.2 Pharmacokinetic properties

Pregabalin

pregabalin is rapidly absorbed when administered in the fasted state, Pregabalin oral bioavailability is estimated to be ≥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.

Methylcobalamin

It 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.

Pyridoxine Hydrochloride

Pyridoxine is absorbed from the GI tract and is converted to the active form pyridoxal phosphate.

It is excreted in the urine as 4-pyridoxic acid.

Folic Acid

Folic acid is rapidly absorbed in the proximal portion of the small intestine. After oral administration, the Cmax can be achieved within one hour. As tetrahydrofolic acid derivative, folic acid is well-distributed in all over the body tissues and stored in hepatic tissues. Folic acid is metabolized in liver into dihydrofolate and tetrahydrofolate forms. About 90% of the administered dose is excreted via 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.

5.3 Preclinical safety data

Not Stated.

6. Pharmaceutical particulars

6.1 List of excipients

Colloidal Silicon Dioxide, Hydroxy Propyl Methyl Cellulose E-15, Ethyl Cellulose 20 CPS, Polyethylene Glycol 400, Isopropyl Alcohol, Methylene Chloride, Dicalcium Phosphate, Microcrystalline Cellulose, Croscarmellose Sodium, Purified Talc, Sodium Lauryl Sulphate, Magnesium Stearate

6.2 Incompatibilities

None Stated.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

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

Keep out of reach of children.

6.5 Nature and contents of container

3 x 10 Alu-Alu Blister Packing.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

NAFDAC Reg No: B4-8251

7. Marketed in Nigeria by

Geneith Pharm. Limited
12 Adewale Crescent,
Off Oshodi-Apape Exp. Way
Oshodi, Lagos-Nigeria

8. Manufactured by

M/s Innova Captab Ltd.
81-B, EPIP, Phase-I, Jharmajri
Baddi-173205, Distt. Solan, HP