1.6.1.1 Name of the medicinal Product

Cinnarizine Tablets 25 mg

1.6.1.1.1 strength

25 mg/Tablet

1.6.1.1.2 Pharmaceutical Form

Oral Tablet

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Cinnarizine BP

1.6.1.2.2 Quantitative declaration

Sr. No.	Ingredients Chemical Name	Specification	Standard Quantity (w/v)	Reason for Inclusion
01	Cinnarizine	BP	25.000	Anti Histaminic
02	Lactose Monohydrate (Supertab 30 GR)	USP-NF	100.00	Diluent
03	Microcrystalline cellulose (PH 102)	BP	40.000	Diluent
04	Crospovidone (Polyplasdone)	USP-NF	5.000	Binder
05	Colloidal Anhydrous Silica (Aerosil)	BP	2.000	Disintegrant
06.	Maize Starch	BP	10.000	Disintegrant
07	Magnesium Stearate	BP	3.000	Lubricant

1.6.1.3 Pharmaceutical Form

Oral Tablet

A White to off-white Coloured, round shaped, flat, uncoated tablet, break-line on one side and plain on other side.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

Cinnarizine tablet indicate for control of vestibular symptoms of both peripheral and central origin and of labyrinthine disorders including vertigo, dizziness, tinnitus, nystagmus, nausea and vomiting. It is also used for prophylaxis of motion sickness.

1.6.1.4.2 Posology and Method of Administration

Cinnarizine tablet 25 mg should preferably be taken after meals.

Adults and children over the age of 12 years:

Peripheral circulatory disorders: 2-3 tablets (50 mg- 75 mg) two to three times daily.

Disorders of balance: One tablet (25 mg) three times daily.

The maximum recommended dosage should not exceed 225 mg (9 tablets) daily. If necessary, the dosage may be divided over 2 or 3 intakes per day. As the effect of Cinnarizine tablets on vertigo is dose dependent, the dosage should be increased progressively.

Motion Sickness:

Adults: One tablet of 25 mg half an hour before traveling; to be repeated every 6 hours.

Children 8 to 12 years: Haifa tablet (12.5 mg) three times daily when necessary.

1.6.1.4.3 Contraindications

Cinnarizine Tablets are contra-indicated in patients with known hypersensitivity to cinnarizine.

1.6.1.4.4 Special Warnings and Special Precautions for Use

As with other antihistamines, cinnarizine may cause epigastric discomfort; taking it after meals may diminish gastric irritation.

In patients with Parkinson's disease, Cinnarizine should only be given if the advantages outweigh the possible risk of aggravating this disease.

Use of Cinnarizine should be avoided in porphyria.

There have been no specific studies in hepatic or renal dysfunction. Cinnarizine should be used with care in patients with hepatic or renal insufficiency.

Cinnarizine may cause somnolence, especially at the start of treatment. Therefore caution should be taken when alcohol, central nervous system (CNS) depressants or tricyclic antidepressants are used concomitantly.

Effects on ability to drive and use machines: Cinnarizine may cause drowsiness, especially at the start of treatment; patients affected in this way should not drive or operate machinery.

Pregnancy: The safety of Cinnarizine in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects. As with other drugs, it is not advisable to administer Cinnarizine in pregnancy.

Lactation: There are no data on the excretion of Cinnarizine in human breast milk; use of Cinnarizine is not recommended in nursing mothers.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

Concurrent use of alcohol, CNS depressants or tricyclic antidepressants may potentiate the sedative effects of either these drugs or of Cinnarizine.

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy: The safety of Cinnarizine in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects. As with other drugs, it is not advisable to administer Cinnarizine in pregnancy.

Lactation: There are no data on the excretion of Cinnarizine in human breast milk; use of Cinnarizine is not recommended in nursing mothers.

1.6.1.4.7 Effects on ability To Drive and use Machines

Effects on ability to drive and use machines: Cinnarizine may cause drowsiness, especially at the start of treatment; patients affected in this way should not drive or operate machinery.

1.6.1.4.8 Undesirable Effects

Immune system disorders: Hypersensitivity.

Nervous system disorders: Somnolence, dyskinesia, extrapyramidal disorder, parkinsonism, tremor.

Gastrointestinal disorders: Gastrointestinal disorder; dry mouth.

Skin and subcutaneous tissue disorders: Lichen planus, subacute cutaneous lupus erythematosus, lichenoid keratosis.

Musculoskeletal and connective tissue disorders: Muscle rigidity.

1.6.1.4.9 Overdose

Symptoms: Acute Cinnarizine overdoses have been reported with doses ranging from 90 to 2,250 mg. The most commonly reported signs and symptoms associated with overdose of Cinnarizine include: alterations in consciousness ranging from somnolence to stupor and coma, vomiting, extrapyramidal symptoms, and hypotonia. In a small number of young children, seizures developed. Clinical consequences were not severe in most cases, but deaths have been reported after single and polydrug overdoses involving Cinnarizine.

Treatment: There is no specific antidote. For any overdose, the treatment is symptomatic and supportive care.

Activated charcoal may be given if considered appropriate.

1.6.1.5 Pharmacological Properties

Cinnarizine's action in the treatment of peripheral vascular disease is due to its anti-vasoconstrictor properties, its action on blood hyperviscosity and its anti-ischacmic effect. Anti-vasoconstriction is thought to be through a calcium blocker mechanism and is evident selectively in vascular smooth muscle. Increased peripheral muscle blood flow may be mediated by prevention of calcium entry into ischaemic erythrocytes, thereby preserving flexibility.

Pharmacokinetic Properties

Absorption: The peak plasma levels of cinnarizine are obtained I to 3 hours after intake.

Distribution: The plasma prote in binding of cinnarizine is 91%.

Metabolism: Cinnarizine is extensively metabolized mainly via CYP2D6 in the liver.

Elimination: The reported elimination half-life for cinnarizine ranges from 4 to 24 hours. The elimination of metabolites occurs as follows: about one third in the urine and two thirds in the faeces. Plasma elimination half life is 3 to 4 hours.

1.6.1.5.1 Preclinical Safety Data

Nonclinical safety studies showed that effects were observed only after chronic exposures from approximately 7 to 35 times the recommended maximum daily human dose of 90 mg/day calculated on a body surface area basis. Cinnarizine blocked the cardiac hERG channel in vitro, however in isolated cardiac tissue and following intravenous application in guinea-pigs, no QTc prolongation or proarrhythmic effects were observed at substantially higher exposures than those expected clinically.

In reproductive studies in the rat, rabbit, and dog, there was no evidence of adverse effects on fertility and no teratogenicity. At high doses associated with maternal toxicity in the rat there was a decreased litter size, an increase in resorptions and a decrease in foetal birth weight.

In vitro mutagenicity studies indicated that the parent compound is not mutagenic however, after reacting with nitrite and forming the nitrosation product, a weak mutagenic activity was observed.

Carcinogenicity studies have not been conducted however, no pre-neoplastic changes were evident during chronic 18-month oral administration in rats up to approximately 35 times the maximum human dose level.

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

Lactose Monohydrate

Microcrystalline cellulose

Crospovidone (Polyplasdone)

Colloidal Anhydrous Silica (Aerosil)

Maize Starch

Magnesium Stearate

1.6.1.6.2 Incompatibilities

Not applicable.

1.6.1.6.3 Shelf Life

24 months

1.6.1.6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

1.6.1.6.5 Nature and Contents of Container

10 Tablets are packed in a blister Pack. Such 10 blisters are packed in a printed carton along with packing insert.

1.6.1.6.6 Special precaution for disposal and other handling

Not Required.

1.6.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

1.6.1.7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.6.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.6.1.10 **Date of Revision of the Text**

1.6.1.11 Dosimetry (If Applicable)

Not Applicable