PACKAGE INSERT TEMPLATE FOR CINNARIZINE TABLET

Brand or Product Name
[Product name] Tablet 25mg

Name and Strength of Active Substance(s)
Cinnarizine 25mg

Product Description
[Visual description of the appearance of the product (eg colour, markings etc)]
eg White, circular flat beveled edge tablets marked '25' on one side

Pharmacodynamics

Cinnarizine is a piperazine derivative, H1 histamine antagonist.

Cinnarizine is a polyvalent non-competitive antagonist of vasoconstrictive agents, and reduces the vascular response to epinephrine, norepinephrine, serotonin, angiotensin, dopamine, and other vasoactive hormones. It is a long-acting, potent inhibitor of potassium chloride-depolarization-induced peripheral vasoconstriction, acting via selective inhibition of calcium influx into depolarized cells, thereby reducing the availability of free calcium ions for induction and maintenance of contraction in smooth muscle.

Cinnarizine directly antagonizes the stimulated influx of extracellular calcium, modifying intracellular calcium adenosine triphosphate balance in erythrocytes, thus increasing their flexibility and decreasing whole blood viscosity. Cinnarizine may further improve deficient microcirculation by increasing erythrocyte deformability and decreasing blood viscosity. Cellular resistance to hypoxia is increased.

Cinnarizine also exhibits anti-spasmodic activity, and decreases night pain and cramps in patients with intermittent claudication. Cinnarizine does not appear to affect sympathetic reflexes, resting blood pressure, pulse rate, or cause orthostatic hypotension, and does not cause a steal effect in patients with intermittent claudication.

Cinnarizine inhibits stimulation of the vestibular system, which results in suppression of nystagmus and other autonomic disturbances. Acute episodes of vertigo can be prevented or reduced by cinnarizine.

Pharmacokinetics
Absorption
Cinnarizine is fairly rapidly absorbed. It is absorbed from the gastrointestinal tract and peak plasma concentrations occur 2 to 4 hours after oral doses.

Absorption from the gastrointestinal tract depends on gastric acidity, which widely varies between patients and explains the variation in oral cinnarizine bioavailability.

Distribution
The plasma protein binding of cinnarizine is 91%.

Metabolism
Cinnarizine is extensively metabolized in the liver via glucuronidation

Elimination
The reported elimination half-life for cinnarizine ranges from 4 to 24 hours. Cinnarizine has an elimination half-life of 3-6 hours. Cinnarizine is excreted in the faeces mainly as unchanged drug, and in the urine predominantly as metabolites.

Indication

- Maintenance therapy for symptoms of labyrinthine disorders, including vertigo, dizziness, tinnitus, nystagmus, nausea and vomiting.
- Prophylaxis of motion sickness
- Prophylaxis of migraine
- Maintenance therapy for symptoms of cerebrovascular origin, including dizziness, ear buzzing (tinnitus), vascular headache, unsociability, and irritability disorders, loss of memory and lack of concentration.
- Maintenance therapy for symptoms of peripheral-circulatory disorders, including Reynaud's phenomenon, acrocyanosis, intermittent claudication, trophic disturbances, trophic and varicose ulcers, paraesthesia, nocturnal cramps, cold extremities.

Recommended Dosage

Cerebral circulatory disorders: 25mg three times a day
Peripheral circulatory disorders: 25mg three times a day
Disorders of balance: 25mg three times a day
Motion sickness:

- in adults: 25mg half an hour before travelling; to be repeated every 6 hours;
- in children; half of the adult dose is recommended.

Cinnarizine should preferably be taken after meals.

The maximum recommended dosage should not exceed 225mg daily. As the effect of Cinnarizine on vertigo is dose dependent, the dosage should be increased progressively.

Mode of Administration
Oral

Contraindications

Cinnarizine is contraindicated in patients with known hypersensitivity to the drug

Warnings and Precautions

Cinnarizine may cause epigastric distress; should be preferably taken after meals to minimize gastric irritation symptoms

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

Cinnarizine may cause somnolence, especially at the start of treatment. Therefore caution should be taken when alcohol or CNS depressants are used concomitantly.

Alcoholic drinks should be avoided.

Effects on Ability to Drive and Use Machines
Since somnolence/ drowsiness may occur especially at the start of treatment, caution should be taken during driving or operating dangerous machinery.

Interactions with Other Medicaments

Procarbazine: CNS depression; to minimize CNS depression and possible potentiation, coadministration of procarbazine and antihistamines should be used with caution

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

Diagnostic Interference: Because of its antihistamine effect, Cinnarizine may prevent otherwise positive reactions to dermal reactivity indicators if used up to 4 days prior to skin testing.

Statement on Usage During Pregnancy and Lactation

Pregnancy
Cinnarizine should be used during pregnancy only if the therapeutic benefits justify the potential risks for the fetus.

Lactation
Nursing should be discouraged in women using Cinnarizine as there are no data on the excretion of Cinnarizine in human breast milk.

Adverse Effects / Undesirable Effects

- *Dermatologic*: Lichen Ruber Planus
- *Endocrine/Metabolic Effects*: weight gain
- *Gastrointestinal Effects*: gastrointestinal disorders, epigastric pain, nausea, vomiting
- *Neurologic Effects*: fatigue, drowsiness, dizziness, asthenia, headache, extrapyramidal symptoms such as tremor, rigor, and hypokinesia
- *Immunologic Effects*: drug-induced Systemic lupus erythematosus

Overdose and Treatment
Symptoms
The following signs and symptoms may occur in the event of Cinnarizine overdosage: alterations in consciousness ranging from somnolence to stupor and coma, vomiting, extrapyramidal symptoms, and hypotonia. In a small number of young children, seizures developed.

Treatment
There is no specific antidote. For any overdose, the treatment is symptomatic and supportive care. Gastric lavage and administration of activated charcoal are recommended**.**

Storage Conditions
[eg Store below…. °C]

Dosage Forms and Packaging Available
[Packaging type & pack size]

Name and Address of Manufacturer
[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder
[Name & full address of marketing authorization holder]

Date of Revision of Package Insert
[day/month/year]