VERTIDIZ Tablets

1. Generic Names

Cinnarizine

Dimenhydrinate

2. Qualitative and Quantitative Composition

Each tablet contains

Cinnarizine	20mg
Dimenhydrinate	40mg

3. Dosage form and strength

Tablets containing Cinnarizine 20mg, Dimenhydrinate 40mg for oral administration.

4. Clinical particulars

4.1 Therapeutic indication

Vertidiz tablets are indicated in treatment of vertigo of:

- Peripheral origin like Benign Paroxysmal positional vertigo (BPPV)
- Central origin associated with Migraine

4.2 Posology and method of administration

One tablet TID.

4.3 Contraindication

Vertidiz tablets are contraindicated in patients with:

- Parkinson's disease.
- History of severe depression.

4.4 Special warnings and precautions for use

- Cinnarizine is contraindicated in liver or kidney disorders and porphyria.
- Vertidiz may impair ability to drive or operate heavy machinery
- Vertidiz must be used with caution in patients with seizures, angle-closure glaucoma, enlargement of prostate gland, asthma, emphysema, acute hepatic insufficiency

4.5 Drug interactions

- Cinnarizine has clinically important, potentially hazardous interactions with alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives, tranquilizers, tricyclic antidepressants

- Dimenhydrinate interacts with

  ✓ MAO inhibitors ,

  ✓ Narcotic pain relievers like codeine,

  ✓ Antibiotics such as gentamicin and vancomycin

  ✓ Antispasmodics like atropine,

  ✓ Belladonna alkaloids

  ✓ Medications that treat Parkinson's disease such as benztropine and trihexyphenidyl.

4.6 Use in special population

- Pediatric: It should be avoided in children.
- Geriatric: It may cause cognitive issues in elderly patients.
- Liver impairment: Contraindicated.
- Renal failure: Contraindicated.
- Pregnancy and lactation: Pregnancy category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. A decision should be made whether to discontinue

breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Vertidiz is known.

4.8 Undesirable effects

- Cinnarizine: Thrombocytopenia, Palpitations, Vertigo, Periorbital oedema, Eyelid oedema , Nausea , Vomiting, Dry mouth, Diarrhoea, Abdominal pain, Back pain, Myalgia, Pain in extremity, Arthralgia, Depression, Insomnia, Dyspnoea, Rash, Urticaria, Pruritus,
- Dimenhydrinate: Palpitations, Tachycardia, Vertigo, Periorbital oedema , Nausea , Vomiting, Dry mouth, Diarrhoea, Abdominal pain, Dyspepsia, Muscular weakness, Hallucination, Dysuria, Dyspnoea, Fixed eruption, Rash, Urticaria, Pruritus, Hypotension

4.9 Overdose

There is limited experience of overdose with Vertidiz Tablets. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

Cinnarizine has two modes of action.

- It acts as an antihistamine drug. It binds to histamine H1 receptors, blocking them and not allowing histamine of the body to activate the receptors. Thus the action of histamine is blocked.
- The second mode of action of Cinnarizine is as a calcium channel blocker. It selectively blocks the influx of calcium ions through the cell membranes. This causes reduced sensitivity of vestibular receptors and causes a reduction in motion induced

dizziness symptoms. Calcium channel blockers also have a role in the prevention of a migraine.

Dimenhydrinate is a competitive antagonist at the histamine H1 receptor, which is widely distributed in the human brain. Dimenhydrinate's anti-emetic effect is probably due to H1 antagonism in the vestibular system in the brain.

5.2 Pharmacodynamics properties

Cinnarizine is an antihistamine and a calcium channel blocker. Histamines mediate a number of activities such as contraction of smooth muscle of the airways and gastrointestinal tract, vasodilatation, cardiac stimulation, secretion of gastric acid, promotion of interleukin release and chemotaxis of eosinophil and mast cells. Competitive antagonists at histamine H1 receptors may be divided into first (sedating) and second (non-sedating) generation agents. Some, such as Cinnarizine also block muscarinic acetylcholine receptors and are used as anti-emetic agents. Cinnarizine through its calcium channel blocking ability also inhibits stimulation of the vestibular system.

Dimenhydrinate is an antiemetics drug combination that contains diphenhydramine and theophylline. It is not effective in the treatment of nausea associated with cancer chemotherapy. Dimenhydrinate directly inhibits the stimulation of certain nerves in the brain and inner ear to suppress nausea, vomiting, dizziness, and vertigo. Diphenhydramine and dimenhydrinate both reduce vestibular neuronal excitation due to angular or linear acceleration motions.

5.3 Pharmacokinetic properties

Cinnarizine is absorbed from the gastrointestinal tract, peak plasma concentrations occurring 2 to 4 hours after oral doses. It undergoes metabolism and has a half-life of 3 to 6 hours. Cinnarizine is excreted in the faeces mainly as unchanged drug, and in the urine predominantly as metabolites.

Dimenhydrinate is well absorbed orally and 98-99% protein bound. Metabolized by cytochrome P450 system and half-life is 1-4 hours.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

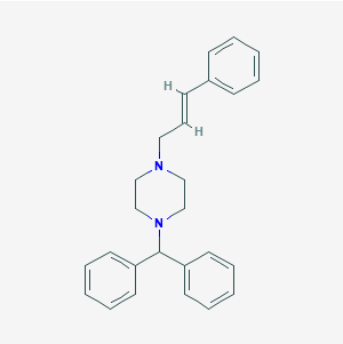
Cinnarizine is a N-alkylpiperazine. It has a role as an antiemetic, a histamine antagonist, a calciumchannel blocker, a muscarinic antagonist, an anti-allergic agent and a H1-receptor antagonist.

Chemical Name: 1-benzhydryl-4-[(*E*)-3-phenylprop-2-enyl]piperazine

Molecular weight: 368.5 g/mol

Molecular formula: $C_{26}H_{28}N_2$

Structure:



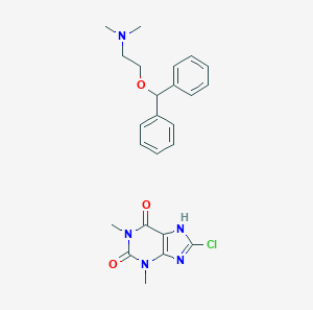
Dimenhydrinate is an ethanolamine and first-generation histamine antagonist with anti-allergic activity.

Chemical Name: 2-benzhydryloxy-*N*,*N*-dimethylethanamine;8-chloro-1,3-dimethyl-7*H*-purine-2,6-dione

Molecular weight: 470 g/mol

Molecular formula: $C_{24}H_{28}ClN_5O_3$

Structure:



8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months

8.3 Packaging Information

Vertidiz tablets are available in blister pack of 10 tablets.

8.4 Storage and handling instructions

Store in cool and dry place.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by The Madras Pharmaceuticals .

11. Details of permission or license number with date

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12. Date of revision: January 2022