SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cinnarizine 15 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 15 mg of cinnarizine.

Excipient with known effect:
Each tablet contains 162.5 mg lactose anhydrous

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, flat bevel edged tablets marked “G” on both sides

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Disorders of balance - maintenance therapy for symptoms of labyrinthine disorders, including vertigo, tinnitus, nystagmus, nausea and vomiting such as is seen in Meniere's Disease.

Cinnarizine is also effective in the control of motion sickness.

4.2 Posology and method of administration

Cinnarizine is for oral administration to both adults and children according to the following dosage regime.

Posology

Vestibular symptoms:
Adults, elderly and children over 12 years:
Two tablets three times a day.

Children 5-12 years:

One tablet three times a day.

The stated doses should not be exceeded.

Motion sickness:
Adults, elderly and children over 12 years:
Two tablets two hours before travel and one tablet every eight hours during journey if necessary.

Children 5-12 years:
One tablet two hours before travel and half a tablet every eight hours during journey if necessary.

Method of administration
For oral use.
Cinnarizine should preferably be taken after meals. The tablets may be sucked, chewed or swallowed whole with water.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

As with other antihistamines, cinnarizine may cause epigastric discomfort; taking it after meals may diminish gastric irritation. Cinnarizine should only be given to patients with Parkinson's disease if the advantages outweigh the possible risk of aggravating this disease.

Because of its antihistamine effect, cinnarizine may prevent an otherwise positive reaction to dermal reactivity indicators if used within 4 days prior to testing.

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 Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 these drugs or of cinnarizine.

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.

Breast-feeding
There are no data on the excretion of cinnarizine in human breast milk. Taking cinnarizine whilst breast-feeding is not recommended.

4.7 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.

4.8 Undesirable effects

The safety of cinnarizine was evaluated in 303 cinnarizine-treated subjects who participated in 6 placebo-controlled trials for the indications peripheral circulatory disorders, cerebral circulatory disorders, vertigo and control of motion sickness ; and in 937 cinnarizine-treated subjects who participated in six comparator and 13 open label clinical trials for the indications peripheral circulatory disorders, cerebral circulatory disorders and vertigo. Based on pooled safety data from these clinical trials, the most commonly reported (>1% incidence) Adverse Drug Reactions (ADRs) were: somnolence (9.9), nausea (3.0) and increased weight (1.5).

Including the above mentioned ADRs, the following ADRs have been observed from clinical trials and post-marketing experiences reported with the use of cinnarizine. Frequencies displayed use the following convention:

Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000) and not known (cannot be estimated from the available data).

System organ class			**Adverse drug reactions**	
			Frequency category	
	Common (≥ 1/100 to < 1/10)	**Uncommon** (≥ 1/1,000 to < 1/100)	**Rare (≥ 1/10,000 to <1/1,000)**	**Not known**
Nervous system disorders	Somnolence	Hypersomnia		Dyskinesia, extrapyramidal disorder,, Parkinsonism, Tremor
Gastrointestinal disorders	Nausea,	Vomiting	Upper abdominal pain, Dyspepsia	
Hepatobiliary disorders				Cholestatic jaundice

Skin and subcutaneous tissue disorders		Hyperhidrolysis, Lichenoid keratosis including lichen planus		Subacute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders				Muscle rigidity
General disorders and administrative site conditions		Fatigue		
Investigations	Weight increased			

Cases of hypersensitivity, headache and dry mouth have also been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA yellow card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
The signs and symptoms are mainly due to the anticholinergic (atropine-like) activity of cinnarizine.

Acute cinnarizine overdoses have been reported with doses ranging from 90 to 2,250 mg. Alterations in consciousness ranging from somnolence to stupor and coma, vomiting, extrapyramidal symptoms and hypotonia are the most commonly reported signs and symptoms associated with a cinnarizine overdose. 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 to cinnarizine and in the event of overdosage, treatment is symptomatic and supportive care.

It is advisable to contact a poison control centre to obtain the latest recommendations for the management of an overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivertigo preparations, ATC code: N07CA02.

Mechanism of action
Cinnarizine has been shown to be a non-competitive antagonist of the smooth muscle contractions caused by various vasoactive agents including histamine. It acts on smooth muscle by selectively inhibiting the transport of calcium ions across cell membranes into depolarised cells, therefore reducing the availability of free Ca^{+} ions for the induction and maintenance of contraction.

Clinical efficacy and safety
Vestibular eye reflexes induced by caloric stimulation of the labyrinth in guinea pigs are markedly depressed by cinnarizine.

Cinnarizine has been shown to inhibit nystagmus.

5.2 Pharmacokinetic properties

In animals, cinnarizine is extensively metabolised, N-dealkylation being the major pathway. Approximately two thirds of the metabolites are excreted with the faeces, the rest in the urine, mainly during the first five days after a single dose.

Absorption
In man, after oral administration, absorption is relatively slow, peak serum concentrations occurring after 2.5 to 4 hours.

Distribution
The plasma protein binding of cinnarizine is 91%

Biotransformation

Cinnarizine undergoes extensive metabolism mainly via CYP2D6 but there is considerable interindividual variation in the extent of metabolism.

Elimination
Approximately two thirds of the metabolites are excreted with the faeces, the rest in the urine (unchanged as metabolites and glucuronide conjugates), mainly during the first five days after a single dose.

The reported elimination half-life for cinnarizine ranges from 4 to 24 hours.

5.3 Preclinical safety data

Nonclinical safety studies showed that effects were observed only after chronic exposures that were 10 – 160 times the recommended maximum daily human dose of 100 mg/day calculated on a body surface area basis, calculated as 2mg/kg as based on a 50 kg person. 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch, maize,
Lactose anhydrous,
Mannitol,
Magnesium stearate,
Talc.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVdC coated PVC blister strips with aluminium foil lidding – 4, 6, 8, 10, 15, 20, 84 and 100

Polypropylene container with tamper-evident polyethylene closure – 4, 6, 8, 10, 15, 20, 84 and 100

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Generics (U.K.) Limited T/A Viatris,
Station Close,
Potters Bar,
EN6 1TL,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 04569/0476

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/06/2003 / 22/01/2009

10 DATE OF REVISION OF THE TEXT

08/05/2026