SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Stugeron 15mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cinnarizine 15 mg
Excipients with known effect: lactose monohydrate and sucrose.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

White, circular biconvex tablets marked S/15 on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Stugeron is effective in the control of motion sickness.

4.2 Posology and method of administration

Posology

Stugeron should preferably be taken after meals.

Adults, elderly and children over 12 years:
2 tablets 2 hours before you travel and 1 tablet every 8 hours during your journey.

Children 5 to 12 years:
One half the adult dose.

Method of administration: Oral

4.3 Contraindications

Stugeron should not be given to patients with known hypersensitivity to cinnarizine or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

In patients with Parkinson's disease, Stugeron 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. Stugeron should be used with care in patients with hepatic or renal insufficiency.

Patients with rare hereditary problems of fructose or galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency, should not take this medicine because it contains lactose and sucrose.

Stugeron 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. Please also refer to section 4.5 Interaction with other medicinal products and other forms of interaction.

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

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 of these drugs or of Stugeron.

Diagnostic interference
Because of its antihistamine effect, Stugeron may prevent otherwise positive reactions to dermal reactivity indicators if used up to 4 days prior to skin testing. Also refer to section 4.4 Special warnings and precautions for use.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of Stugeron 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 Stugeron in pregnancy.

Lactation
There are no data on the excretion of Stugeron in human breast milk. Use of Stugeron is not recommended in nursing mothers.

4.7 Effects on ability to drive and use machines

Stugeron 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 Stugeron (30-225mg/day) was evaluated in 601 subjects (of which 303 were treated with Stugeron, 298 were given placebo) who participated in 6 placebo-controlled, double-blind clinical trials; 2 in the treatment of peripheral circulatory disorders, 1 in the treatment of cerebral circulatory disorders, 1 in the treatment of vertigo, 1 in the prevention of motion sickness, and 1 in the treatment of both vertigo and cerebral circulatory disorders.

Six comparator trials and 13 open-label clinical trials were selected to determine the incidence of adverse reactions. In 19 studies, 937 subjects were treated with doses ranging from 25 to 450 mg/day Stugeron, in the treatment of 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%) and Weight Increased (1.5%).

Including the above-mentioned ADR, the following ADRs have been observed from clinical trials and post-marketing experiences reported with the use of Stugeron 15mg Tablets. 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), 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)	**Not Known**
Nervous System Disorders	Somnolence		Dyskinesia; Extrapyramidal Disorder; Parkinsonism; Tremor
Gastrointestinal disorders	Nausea; Dyspepsia	Vomiting; Abdominal Pain Upper	
Hepatobiliary disorders			Cholestatic Jaundice
Skin and subcutaneous tissue disorders		Hyperhidrosis; Lichenoid Keratosis including Lichen Planus	Subacute Cutaneous Lupus Erythematosus
Musculoskeletal and Connective Tissue Disorders			Muscle rigidity
General Disorders and Administration Site Conditions		Fatigue	

Investigations	Weight Increased		

Cases of hypersensitivity, headache and dry mouth have 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 2,250mg. 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.

Management
There is no specific antidote. For any overdose, the treatment is symptomatic and supportive care. It is advisable to contact a poison control centre to obtain the latest recommendation for the management of an overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivertigo preparations, ATC code: N07CA02

Cinnarizine has been shown to be a non competitive antagonist of the smooth muscle contractions caused by various vasoactive agents including histamine.

Cinnarizine also acts on vascular smooth muscle by selectively inhibiting the calcium influx into depolarized cells, thereby reducing the availability of free Ca2+ ions for the induction and maintenance of contraction.

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 is extensively metabolised mainly via CYP2D6, but there is considerable inter-individual variation in the extent of metabolism.

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

The elimination of metabolites occurs as follows: one third in the urine (unchanged as metabolites and glucuronide conjugates) and two-thirds in the faeces.

5.3 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 90mg/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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Sucrose
Talc
Magnesium stearate
Povidone

6.2 Incompatibilities

None known.

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

PVC/aluminium foil blisters of 15 tablets in printed cardboard cartons.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0349

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/09/1999 / 08/09/2005

10 DATE OF REVISION OF THE TEXT

19/12/2022