1 NAME OF THE MEDICINAL PRODUCT
Stugeron 15 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 15 mg cinnarizine.
Excipients with known effect:
Each tablet contains 160 mg lactose monohydrate and 15 mg sucrose.
For the full list of excipients, see section 6.1

3. Pharmaceutical Form
White circular tablet with S/15 on one side and Janssen on the other side.

Clinical Particulars

4.1. Therapeutic Indications
Stugeron is for the control of vestibular disorders such as vertigo, tinnitus, nausea and vomiting such as is seen in Meniere’s Disease.
Stugeron is also effective in the control of motion sickness.

4.2. Posology and Method of Administration
Route of administration
Oral. The tablets may be chewed, sucked or swallowed whole.

Dosage
Stugeron should preferably be taken after meals.

Vestibular symptoms
Adults, elderly and children over 12 years: 2 tablets three times a day.
Children 5 to 12 years: One half the adult dose.
These doses should not be exceeded.

Motion sickness
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.

4.3. Contra-indications

Stugeron should not be given to patients with known hypersensitivity to cinnarizine.

4.4. Special warnings and precautions for use

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

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

Because of its antihistamine effect, Stugeron 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. Stugeron should be used with care in patients with hepatic or renal insufficiency.

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

4.5. Interaction with other medicinal products and other forms of interactions

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

4.6. Fertility, pregnancy and lactation

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.

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 was evaluated in 372 cinnarizine-treated subjects who participated in 7 placebo-controlled trials for the indications peripheral circulatory disorders, cerebral circulatory disorders, vertigo and seasickness; and in 668 cinnarizine-treated subjects who participated in six comparator and thirteen 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 (>2% incidence) Adverse Drug Reactions (ADRs) were: somnolence (8.3) and weight increased (2.1).

Including the above mentioned ADRs, the following ADRs have been observed from clinical trials and post-marketing experiences reported with the use of Stugeron. 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).

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Drug Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency Category</td>
</tr>
<tr>
<td></td>
<td>Common (≥ 1/100 to &lt; 1/10)</td>
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<tr>
<td>Nervous System Disorders</td>
<td>Somnolence</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea; Dyspepsia</td>
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<tr>
<td>Hepato-biliary disorders</td>
<td></td>
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<tr>
<td>Skin and subcutaneous tissue disorders</td>
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<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td></td>
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<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
</tr>
<tr>
<td>Investigations</td>
<td>Weight increased</td>
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</tbody>
</table>

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.

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. 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 should only be considered in patients presenting within one hour of taking a potentially toxic overdose (ie more than 15mg/kg).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 depolarised cells, thereby reducing the availability of free Ca^{2+} 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%.

Metabolism

Cinnarizine is extensively metabolised mainly via CYP2D6, but there is considerable interindividual 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 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 fetal 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.

Pharmaceutical Particulars

6.1. List of Excipients

Lactose monohydrate
Maize starch
Sucrose
Talc
Magnesium stearate
Polyvidone K90
Water

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
or
Polystyrene tubs with polyethylene caps
Each pack containing 15, 25, 100, 250 or 1000 tablets.

6.6 **Special precautions for disposal**
No special requirements.

7 **MARKETING AUTHORISATION HOLDER**

Janssen-Cilag Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8. **Marketing Authorisation Number**

PL 0242/5009R

9. **Date of First Authorisation/Renewal of Authorisation**

Date of First Authorisation: 14 September 1989
Renewal of Authorisation: 23 March 1995

10 **DATE OF REVISION OF THE TEXT**