Special Warnings and Special Precautions for Use
As with other antihistamines STUGERON may cause epigastric distress; 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.

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

Interactions with Other Medicinal Products and Other Forms of Interaction
Alcohol/CNS depressants/Tricyclic Antidepressants: Concurrent use may potentiate the sedative effects of either of these medications 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.

Pregnancy and Lactation
Although in animal studies, STUGERON has shown no teratogenic effects, as with all drugs, STUGERON should be used during pregnancy only if the therapeutic benefits justify the potential risks for the fetus.

There are no data on the excretion of STUGERON in human breast milk: nursing should therefore be discouraged in women using STUGERON.

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

Undesirable Effects
Clinical Trial Data
Placebo-Controlled Double-Blind Data – Adverse Drug Reactions Reported at ≥1% Incidence
The safety of STUGERON (30 to 225mg/day) was
evaluated in 740 subjects (of which 372 were treated with STUGERON, 368 were given placebo) who participated in 7 placebo-controlled, double-blind clinical trials: three in the treatment of peripheral circulatory disorders, one in the treatment of cerebral circulatory disorders, two in vertigo, and one in seasickness. ADRs reported by ≥1% of STUGERON-treated subjects noted in the double-blind clinical trials are shown in Table 1.

### Table 1. Adverse Drug Reactions Reported by ≥1% of STUGERON-treated Subjects in 7 Double-Blind Placebo-Controlled Clinical Trials of STUGERON

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Preferred Term</th>
<th>STUGERON (n=372)</th>
<th>Placebo (n=368)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Somnolence</td>
<td>8.3%</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

**Comparator and Open-Label Data – Adverse Drug Reactions Reported at ≥1% Incidence**

Six comparator trials and thirteen open label trials were selected to determine the incidence of ADRs. In these 19 studies, 668 subjects were treated with doses ranging from 50 to 225 mg/day STUGERON, in the treatment of peripheral circulatory disorders, cerebral circulatory disorders, and vertigo. ADRs reported by ≥1% of STUGERON-treated subjects noted in the comparator and open label clinical trials are shown in Table 2.

### Table 2. Adverse Drug Reactions Reported by ≥1% of STUGERON-treated Subjects in 6 Comparator and 13 Open Clinical Trials of STUGERON

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Preferred Term</th>
<th>STUGERON (n=668)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Nausea</td>
<td>1.5%</td>
</tr>
<tr>
<td></td>
<td>Investigations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Weight increased</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

**Postmarketing Data**

Adverse events first identified as ADRs during postmarketing experience with cinnarizine are included in Tables 4 and 5. The postmarketing review was based on review of all cases where there was a use of cinnarizine (STUGERON). In each table, the frequencies are provided according to the following convention:

- **Very common** ≥1/10
- **Common** ≥1/100 to <1/10
- **Uncommon** ≥1/1000 to <1/100
- **Rare** ≥1/10000 to <1/1000
- **Very rare** <1/10000 including isolated reports

In Table 4, ADRs are presented by frequency category based on spontaneous reporting rates.

### Table 3. Adverse Drug Reactions Reported by <1% of STUGERON-treated Subjects in Either the Placebo- or Comparator-controlled or Open Clinical Trials.

<table>
<thead>
<tr>
<th>Nervous System Disorders</th>
<th>Hypersomnia</th>
<th>Lethargy</th>
<th></th>
</tr>
</thead>
</table>

**Gastrointestinal Disorders**

- Stomach discomfort
- Vomiting
- Abdominal pain upper
- Dyspepsia

**Skin and Subcutaneous Tissue Disorders**

- Hyperhidrosis
- Fatigue

### Table 4: Adverse Drug Reactions Identified During Postmarketing Experience with cinnarizine (STUGERON) by Frequency Category Estimated From Spontaneous Reporting Rates

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Preferred Term</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Dyskinesia</td>
<td>Very rare</td>
</tr>
<tr>
<td></td>
<td>Extrapyramidal disorder</td>
<td>Very rare</td>
</tr>
<tr>
<td></td>
<td>Parkinsonism</td>
<td>Very rare</td>
</tr>
<tr>
<td></td>
<td>Tremor</td>
<td>Very rare</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>Lichenoid keratosis</td>
<td>Very rare</td>
</tr>
<tr>
<td></td>
<td>Lichen planus</td>
<td>Very rare</td>
</tr>
<tr>
<td></td>
<td>Subacute cutaneous lupus erythematosus</td>
<td>Very rare</td>
</tr>
</tbody>
</table>
Table 4: Adverse Drug Reactions Identified During Postmarketing Experience with cinnarizine (STUGERON) by Frequency Category Estimated From Spontaneous Reporting Rates

| Musculoskeletal, Connective Tissue and Bone Disorders | Muscle rigidity | Very rare |

**Overdose**

**Symptoms**

Acute cinnarizine overdoses have been reported with doses ranging from 90 to 2250 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. Within the first hour after ingestion, gastric lavage may be performed. Activated charcoal may be given if considered appropriate.

**Pharmacokinetic Properties**

**Absorption**

The peak plasma levels of cinnarizine are obtained 1 to 3 hours after intake.

**Distribution**

The plasma protein binding of cinnarizine is 91%.

**Metabolism**

Cinnarizine is extensively metabolized mainly via CYP2D6.

**Elimination**

The reported elimination half-life for cinnarizine ranges from 4 to 24 hours. The elimination of these metabolites occurs for about 1/3 in the urine and for 2/3 with the faeces.

**Preclinical Safety Data**

A comprehensive battery of nonclinical safety studies showed that effects were observed only after chronic exposures from approximately 5 to 72 times, on a mg/kg basis when compared to the maximum recommended human dose of 225 mg/day, calculated as 4.5 mg/kg as based on a 50 kg person.

**PHARMACEUTICAL PARTICULARS**

**List of Excipients**

*25 mg tablets*

Lactose, maize starch, sucrose, talc, hydrogenated vegetable oil, polyvidone (formulation F50).

**Incompatibilities**

None known.

**Shelf Life**

Observe expiry date on the outer pack.

**Special Precautions for Storage**

Tablets: store between 15°C - 30°C. Keep out of reach of children.
Nature and Contents of Container
Blister packs with 25 mg tablets.

Instructions for Use and Handling <and Disposal>
No special requirements.

MANUFACTURED BY
See outer carton.

DATE OF REVISION OF THE TEXT
March 2009