NAME OF THE MEDICINAL PRODUCT
STUGERON®

DOSAGE FORM AND STRENGTH
Each tablet contains 25 mg cinnarizine.

White, circular, biconvex, halfscored tablet with the inscription "JANSSEN" on one side and "S/25" on the other side.

For excipients, see List of Excipients.

CLINICAL INFORMATION
Indications
- Disorders of balance – maintenance therapy for symptoms of labyrinthine disorders, including vertigo, dizziness, tinnitus, nystagmus, nausea and vomiting.
- Prophylaxis of motion sickness.

Dosage and Administration
Dosage
Disorders of balance – Adults
25 mg tablet: 1 tablet three times a day.

Prophylaxis of motion sickness:
Adults and adolescents aged 13 years and above
- 25 mg tablet: 1 tablet at least half an hour before travelling; to be repeated every 6 hours.

Children aged 6 to 12 years:
- Half of the adult dose is recommended.

Administration
STUGERON® should preferably be taken orally after meals.

Contraindications
STUGERON® is contraindicated in patients with known hypersensitivity to the drug.

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,central nervous system (CNS) depressants or tricyclic antidepressants are used concomitantly.

Interactions with Other Medicinal Products and Other Forms of Interaction
Alcohol, CNS depressants and Tricyclic Antidepressants:
The sedative effects of STUGERON® and of any of the following may be potentiated when used concomitantly: alcohol, CNS depressants, or tricyclic antidepressants.

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 Breast-feeding
Pregnancy
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.

Breast-feeding
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.

Adverse Reactions
Throughout this section, adverse reactions are presented. Adverse reactions are adverse events that were considered to be reasonably associated with the use of cinnarizine based on the comprehensive assessment of the available adverse event information. A causal relationship with cinnarizine cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Clinical Trial Data
Placebo-Controlled Double-Blind Data – Adverse Reactions Reported at ≥1% Incidence
The safety of STUGERON® (30 to 225 mg/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.

Adverse reactions reported by ≥1% of STUGERON®-treated subjects noted in the double-blind clinical trials are shown in Table 1.

Table 1. Adverse Reactions Reported by ≥1% of STUGERON®-treated Subjects in 6 Double-Blind Placebo-Controlled Clinical Trials of STUGERON®

System/Organ Class Preferred Term	**STUGERON®** **(n=303)** **%**	**Placebo** **(n=298)** **%**
Nervous System Disorders		
Somnolence	9.9	5.4
Gastrointestinal Disorders		
Nausea	3.0	1.7

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

Six comparator trials and 13 open-label trials were selected to determine the incidence of adverse reactions. In these 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.

Adverse reactions reported by ≥1% of STUGERON®-treated subjects noted in the comparator and open label clinical trials are shown in Table 2.

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

System/Organ Class Preferred Term	**STUGERON®** **(n=937)** **%**
Investigations	
Weight increased	1.5

Placebo, Comparator, and Open-Label Data – Adverse Reactions Reported at <1% Incidence

Additional adverse reactions that occurred in <1% of STUGERON®-treated subjects in the above 2 clinical datasets (25 studies with a total of 1240 subjects treated with doses ranging from 25 to 450 mg/day) are listed below in Table 3.

Table 3. Adverse Reactions Reported by <1% of STUGERON®-treated Subjects in Placebo-controlled, Comparator-controlled, and Open-label Clinical Trials of STUGERON®

System/Organ Class Preferred Term	**STUGERON®** **(n=1240)** **%**
Nervous System Disorders	
Hypersomnia	0.16
Gastrointestinal Disorders	
Vomiting	0.24
Abdominal pain upper	0.08
Dyspepsia	0.08
Skin and Subcutaneous Tissue Disorders	
Hyperhidrosis	0.32
General Disorders and Administration Site Conditions	
Fatigue	0.40

Postmarketing Data

Adverse events first identified as adverse reactions during postmarketing experience with cinnarizine are included in Table 4. The postmarketing review was based on review of all cases where there was a use of cinnarizine. Frequencies in this table are provided according to the following convention:

Very common	≥1/10 (≥10%)
Common	≥1/100 and <1/10 (≥1% and < 10%)
Uncommon	≥1/1000 and <1/100 (≥ 0.1% and < 1%)
Rare	≥1/10000 and <1/1000 (≥0.01 and < 0.1%)
Very rare	<1/10000, including isolated reports (< 0.01%)
Not known	Cannot be estimated from the available data

Table 4: Adverse Reactions Identified During Postmarketing Experience with cinnarizine (STUGERON®) by Frequency Category

System/Organ Class Preferred Term	**Frequency Estimated From Spontaneous Reporting Rates**
Nervous System Disorders	
Dyskinesia	*Very rare*
Extrapyramidal disorder	*Very rare*
Parkinsonism	*Very rare*
Tremor	*Very rare*
Hepatobiliary Disorders	
Jaundice cholestatic	*Very rare*
Skin and Subcutaneous Tissue Disorders	
Lichenoid keratosis	*Very rare*
Lichen planus	*Very rare*
Subacute cutaneous lupus erythematosus	*Very rare*
Musculoskeletal, Connective Tissue and Bone Disorders	
Muscle rigidity	*Very rare*

Overdose

Symptoms and signs

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

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: antivertigo preparations, **ATC code N07CA02**

Mechanism of action
Cinnarizine inhibits contractions of vascular smooth muscle cells by blocking calcium channels.
In addition to this direct calcium antagonism cinnarizine decreases the contractile activity of vasoactive substances, such as norepinephrine and serotonin, by blocking receptor-operated calcium channels. Blockade of the cellular influx of calcium is tissue-selective, and results in anti-vasoconstrictor properties without effect on blood pressure and heart rate.
Cinnarizine may further improve deficient microcirculation by increasing erythrocyte deformability and decreasing blood viscosity. Cellular resistance to hypoxia is increased. Cinnarizine inhibits stimulation of the vestibular system, which results in suppression of nystagmus and other autonomic disturbances. Acute episodes of vertigo can be prevented or reduced by cinnarizine.

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 metabolites is about 1/3 in the urine and 2/3 in the faeces.

Non-clinical Information
A comprehensive battery of nonclinical safety studies showed that effects were observed only after chronic exposures that were 10 to 160 times (on a mg/kg basis) those at the maximum recommended human dose of 100 mg/day, calculated as 2 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
3 years.

Special Precautions for Storage
Tablets: store between 15°C - 30°C.
Keep out of the sight and reach of children.
Protect from light.

Nature and Contents of Container
Blister packs of 200 or 250 tablets.
Not all pack sizes may be available locally.

PRODUCT REGISTRANT
Johnson & Johnson International (Singapore) Pte. Ltd.
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