เอกสารกำกับยาสำหรับแพทย์ภาษาอังกฤษ

STUGERON®

1. Name of the Medicinal Product

STUGERON® (INN: Cinnarizine)

2. Qualitative and Quantitative Composition

Each tablet contains 25 mg cinnarizine.

For excipients, see *List of Excipients.*

3. Pharmaceutical Form

25 mg tablets

White, circular, biconvex, halfscored tablet with the inscription "JANSSEN" on one side and "$\frac{S}{25}$" on the other side.

4. Clinical Particulars

4.1 Therapeutic indication

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

4.2 Posology and method of administration

Dosage

Disorders of balance – Adults

25 mg tablet: 1 tablet three times a day.

Elderly

A causal association between cinnarizine and parkinsonism is unclear from observational studies and no controlled clinical studies have been conducted in elderly patients. Long term use should be avoided, and treatment should be under physician's supervision.

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 after meals.

4.3 Contraindication

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

4.4 Special warning and precautions

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.

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.

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.

4.5 Interaction with other medicinal products and other forms of interactions

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.

4.6 Fertility, pregnancy and lactation

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.

4.7 Effect on ability to drive and use machine

Since somnolence may occur, especially at the start of treatment, caution should be taken during activities such as driving or operating machinery.

4.8 Undesirable effects

The safety of Stugeron 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 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).

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;	
Hepato-biliary disorders				Cholestatic jaundice
Skin and subcutaneous tissue disorders		Hyperhydrosis; Lichenoid keratosis including Lichen planus		Subacute cutaneous lupus erythematosus
Musculoskeletal and Connective Tissue Disorders				Muscle rigidity
General Disorders and		Fatigue		

Administration Site Conditions				
Investigations	Weight increased			

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

4.9 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.

5. Pharmacological Properties

5.1 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.

5.2 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.

5.3 Preclinical Safety Data

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

6. Pharmaceutical Particulars

6.1 List of excipients

25 mg tablets

Cotton seed oil hydrogenated

Lactose monohydrate

Maize starch

Polyvidone

Sucrose

Talc.

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30° C.

Keep out of the sight and reach of children.

6.5 Nature and contents of container

Blister packs with 25 mg tablets. 2x10's and 3x10's.

Date of revision of the text

23 May 2023 (CCDS version 31-May-2019 hybrid with UK SmPC version 22-May-2020 section 4.4, 4.8 and 5.3)

Manufactured by

Lusomedicamenta Sociedade Técnica Farmacêutica, S.A., Barcarena, Portugal

Product Name	Marketing Authorization Numbers	Date of Authorization
STUGERON®	1C 15105/63	30 December 2020

Imported by

Janssen-Cilag Ltd., Bangkok, Thailand

To report Suspected Adverse Reactions, please contact us at aepqcjacth@its.jnj.com

For any product information, please contact us at medinfosea@its.jnj.com