For the use of a Registered Medical Practitioner or a Hospital or Laboratory

Rx

Cinnarizine Tablets I.P.

Stugeron®
Stugeron® Forte

Description

Stugeron/ Stugeron forte is a selective calcium entry blocker belonging to group IV of the calcium antagonists (WHO-classification).

Stugeron/ Stugeron Forte have an anti-histamine (H1)-effect.

Stugeron is available as a white to nearly white, uncoated, round, biconvex tablets with break line on one side and plain on other.

Stugeron is available as oral tablets containing 25 mg cinnarizine.

Stugeron forte is available as a Yellow colored, flat, round, beveled edged uncoated tablet with half scored on one side and “JANSSEN” embossed on the other side.

Stugeron Forte as oral tablets containing 75 mg cinnarizine.

For excipients, see List of Excipients.

Properties

Pharmacodynamic

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 100mg/day, calculated as 2mg/kg as based on a 50 kg person.

Indications

- Prophylaxis of migraine.

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

- Prophylaxis of motion sickness.

Contraindications

Stugeron/ Stugeron Forte is contraindicated in patients with known hypersensitivity to the drug.

Warnings and Precautions

As with other antihistamines Stugeron/ Stugeron Forte 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/ Stugeron Forte 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

Alcohol/CNS depressants/ and tricyclic antidepressants: The sedative effects of Stugeron / Stugeron Forte 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/ Stugeron Forte may prevent otherwise positive reactions to dermal reactivity indicators if used up to 4 days prior to skin testing.

Pregnancy and Lactation

Pregnancy

Although in animal studies, Stugeron/ Stugeron Forte has shown no teratogenic effects, as with all drugs, Stugeron/ Stugeron Forte 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/ Stugeron Forte in human breast milk: nursing should therefore be discouraged in women using Stugeron/ Stugeron Forte.

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.

Dosage and Administration

Dosage

Prophylaxis of migraine: Adults

25 mg tablet: 1 tablet three times a day

75 mg tablet: 1 tablet daily.

Disorders of balance: Adults

25 mg tablet: 1 tablet three times a day

75 mg tablet: 1 tablet daily

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.

Administration

Stugeron/ Stugeron Forte should preferably be taken after meals.

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 drug 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, and 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 Drug Reactions Reported by ≥1% of Stugeron-treated Subjects in 7 Double-Blind Placebo-Controlled Clinical Trials of Stugeron

System/Organ Class	**Stugeron**	**Placebo**
Preferred Term	**(n=303)**	**(n=298)**
	%	**%**

Nervous System Disorders		
Somnolence	9.9	5.4
Gastrointestinal Disorders		
Nausea	3.0	1.7

Comparator and open-label data – adverse drug 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 Clinical Trials of Stugeron

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

Placebo, comparator, and open-label data – adverse drug 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 Either the 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

Post marketing data

Adverse events first identified as adverse reactions during post marketing experience with cinnarizine are included in Table 4. The post marketing 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 Drug Reactions Identified During Post marketing Experience with cinnarizine (Stugeron/ Stugeron Forte) by Frequency Category

System/Organ Class Preferred Term	Frequency Estimated from Spontaneous Reporting Rates	Frequency Estimated from Clinical Trial Data from Stugeron/ Stugeron Forte
Nervous System Disorders		
Dyskinesia	Very rare	Not known
Extrapyramidal disorder	Very rare	Not known
Parkinsonism	Very rare	Not known
Tremor	Very rare	Not known

Hepatobiliary Disorders		
Jaundice cholestatic	Very rare	Not known
Skin and Subcutaneous Tissue Disorders		
Lichenoid keratosis	Very rare	Uncommon
Lichen planus	Very rare	Not known
Subacute cutaneous lupus erythematosus	Very rare	Not known
Musculoskeletal, Connective Tissue and Bone Disorders		
Muscle rigidity	Very rare	Not known

Overdose

Symptoms and signs

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

How supplied

Stugeron: Shelf unit containing 13 Blisters of 2 x 25 tablets each

Stugeron Forte: Shelf unit containing 20 Blisters of 20 tablets each

PHARMACEUTICAL INFORMATION

List of Excipients of Stugeron

The inactive ingredients are Lactose, Sugar, Starch, Povidone, Talc, Magnesium Stearate and Purified Water.

List of Excipients of Stugeron Forte

The inactive ingredients are Lactose, Tartrazine, Starch, Povidone, Magnesium Stearate and Purified Water.

Storage conditions

Store in a dry, well-ventilated place at temperature not exceeding 30°C. Store protected from light.

Keep out of the sight and reach of children.

Made in India by:

Johnson & Johnson Pvt. Ltd.,

Gala No. 3, BULDG No. B-2 Citylink Warehousing Complex,

S.No. 120-121, Mumbai Nashik Highway, Village Vadpe,

Taluka – Bhiwandi -421302, Maharashtra**.**

Manufactured at:

Encore Healthcare Pvt. Ltd.,

Plot No. D-5, M.I.D.C, Industrial Area,

Paithan, Aurangabad – 431148.

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