

Summary of Product Characteristics
(S.P.C)

LORITIN[®]

Loratadine

1. NAME OF THE MEDICINAL PRODUCT

LORITIN[®]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Loratadine 5 mg / 5 ml

Loratadine $C_{22}H_{23}ClN_2O_2$

4-8(chloro-5,5-dihydro-1H-benzo[5,6]cyclohepta[1,2b]pyridin-11-ylidene)-1-piperidinecarboxylic acid ethyl ester

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

LORITIN[®] is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and method of administration

Administration : For oral administration

Dosage:

Adults and children over 12 years of age : 10 ml of syrup (10mg loratadine) once daily .

LORITIN[®] syrup may be taken without regard to mealtime.

Children 2-12 years of age :

Body weight > 30 Kg : 10 ml of syrup (10 mg loratadine) once daily

Body weight ≤ 30 kg : 5ml of syrup (5 mg loratadine) once daily

Safety and efficacy of LORITIN[®] in children under 2 years of age has not been established.

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. No dosage adjustments are required in the elderly or in patients with renal insufficiency.

4.3. Contra-indications

LORITIN[®] is contra-indicated in patients who are hypersensitive to the active substance or to any of the excipients in these formulations.

4.4. Special warnings and special precautions for use

- LORITIN[®] should be administered with caution in patients with severe liver impairment (see 4.2).
- LORITIN[®] syrup contains 600 mg sucrose per 1 ml. This should be taken into account in patients with diabetes mellitus.
- The administration of LORITIN[®] should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

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

- When administered concomitantly with alcohol, LORITIN[®] has no potentiating effects as measured by psychomotor performance studies.
- Due to the wide therapeutic index of Loratadine no clinically relevant interactions are expected and none were observed in the conducted clinical trials (see 5.2).

4.6. Administration during Pregnancy and Lactation

Pregnancy

Loratadine was not teratogenic in animal studies. The safe use of loratadine during pregnancy has not been established. The use of LORITIN[®] during pregnancy is therefore not recommended.

Lactation

Loratadine is excreted in human breast milk. Therefore, its administration to nursing mothers is not recommended.

4.7. Effects on ability to drive and operate machines

In clinical trials that assessed driving ability, no impairment occurred in patients receiving loratadine. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

4.8. Undesirable effects

In clinical trials in a pediatric population of children aged 2 to 12 years, common adverse reactions reported in excess of placebo were headache (2.7%), nervousness (2.3%), and fatigue (1%).

In clinical trials involving adults and adolescents in a range of indications including AR and CIU, at the recommended dose of 10 mg daily, adverse reactions with loratadine were reported in 2% of patients in excess of those treated with placebo. The most frequent adverse reactions reported in excess of placebo were somnolence (1.2%), headache (0.6%), increased appetite (0.5%) and insomnia (0.1%). Other adverse reactions reported very rarely during the post-marketing period are listed in the following table.

Immune disorders	Anaphylaxis
Nervous system disorders	Dizziness
Cardiac disorders	Tachycardia, palpitations
Gastrointestinal disorders	Nausea, dry mouth, gastritis
Hepato-biliary disorders	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Rash, alopecia
General disorders and administration site conditions	Fatigue

4.9. Overdosage

Overdosage with loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported with overdoses.

In the event of overdosage, general symptomatic and supportive measures are to be instituted and maintained for as long as necessary. Administration of activated charcoal as a slurry with water may be attempted. Gastric lavage may be considered. Loratadine is not removed by haemodialysis and it is not known if loratadine is removed by peritoneal dialysis. Medical monitoring of the patient is to be continued after emergency treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines – H₁ antagonist, ATC code: R06A X13.

Loratadine, the active ingredient in LORITIN[®], is a tricyclic antihistamine with selective, peripheral H₁-receptor activity.

Loratadine has no clinically significant sedative or anticholinergic properties in the majority of the population and when used at the recommended dosage.

During long-term treatment there were no clinically significant changes in vital signs, laboratory test values, physical examinations or electrocardiograms.

Loratadine has no significant H₂-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity.

5.2. Pharmacokinetic properties

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP3A4 and CYP2D6. The major metabolite-desloratadine (DL) is pharmacologically active and responsible for a large part of the clinical effect. Loratadine and DL achieve maximum plasma concentrations (T_{max}) between 1-1.5 hours and 1.5-3.7 hours after administration, respectively.

Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin, and cimetidine in controlled trials, but without clinically significant changes (including electrocardiographic)

Loratadine is highly bound (97-99%) and its active metabolite moderately bound (73-76%) to plasma proteins.

In healthy subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours respectively. The mean elimination half-lives in healthy adult subjects were 8.4 hours (range=3 to 20 hours) for loratadine and 28 hours (range=8.8 to 92 hours) for the major active metabolite.

Approximately 40% of the dose is excreted in the urine and 42% in the faeces over a 10 day period and mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. Less than 1% of the active substance is excreted unchanged in active form, as loratadine or DL.

The bioavailability parameters of loratadine and of the active metabolite are dose proportional.

The pharmacokinetic profile of loratadine and its metabolites is comparable in healthy adult volunteers and in healthy geriatric volunteers.

Concomitant digestion of food can delay slightly the absorption of loratadine but without influencing the clinical effect.

In patients with chronic renal impairment, both the AUC and peak plasma levels (C_{max}) increased for loratadine and its metabolite as compared to the AUCs and peak plasma levels (C_{max}) of patients with normal renal function. The mean elimination half-lives of loratadine and its

metabolite were not significantly different from that observed in normal subjects. Haemodialysis does not have an effect on the pharmacokinetics of loratadine or its active metabolite in subjects with chronic renal impairment.

In patients with chronic alcoholic liver disease, the AUC and peak plasma levels (C_{max}) of loratadine were double while the pharmacokinetic profile of the active metabolite was not significantly changed from that in patients with normal liver function. The elimination half-lives for loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

5.3. Preclinical safety data

Preclinical data reveal no special hazard based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In reproductive toxicity studies, no teratogenic effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

No evidence of mucous membrane irritation was observed after daily administration of up to 12 tablets (120 mg) of oral lyophilisates into the hamster cheek pouch for five days.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sucrose, Glycerol, Propylene glycol, Sodium benzoate, Peach flavour, Citric acid monohydrate, Purified water.

6.2. Incompatibilities

Not known

6.3. Shelf life

The shelf life of the product is 36 months under normal conditions.

6.4. Special precautions for storage

LORITIN[®] should be stored at room temperature (< 25°C). Keep the product away from the reach of children.

6.5. Nature and contents of container

Clear, colourless solution in glass, caramel-brown bottle. Each bottle contains 120 ml of syrup.
Each box contains 1 bottle and a patient information leaflet.

6.6 Instructions for use and handling

No special instructions are required for use.

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

To be advised.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be advised.

10. DATE OF REVISION OF THE TEXT

April 2005