PIL OF LORHISTINA SYRUP

13. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Lorhistina 5mg/5mL Syrup

13.1 ***Strength***

5 mg/5 mL

13.2 ***Pharmaceutical form***

Syrup

14. QUALITATIVE AND QUANTITATIVE COMPOSITION

14.1 ***Qualitative declaration***

Sucrose BP, Sodium Benzoate BP, Propylene glycol BP, Glycerin BP, Citric acid anhydrous BP, raspberry berry liquid flavour,

14.2 ***Quantitative declaration***

Loratadine USP	5.00
Sucrose BP	3000.00
Sodium Benzoate BP	5.00
Propylene Glycol BP	500.00
Glycerin BP	550.00
Citric Acid Anhydrous BP	89.61
Raspberry Liquid Flavour	0.050
Purified Water BP	850.34

14.3 ***Salts and hydrates***

NA

14.4 ***Esters and pro-drugs***

NA

14.5 ***Oral powders for solution or suspension***

NA

14.6 ***Parenterals excluding powders for reconstitution***

NA

14.7 ***Powders for reconstitution prior to parenteral administration***

NA

14.8 ***Concentrates***

NA

14.9 ***Transdermal patches***

NA

14.10 ***Multidose solid or semi-solid products***

NA

14.11 ***Biological medicinal products***

NA

14.11.1 ***Expression of strength***

mg

14.11.2 ***The biological origin of the active substance***

NA

14.11.3 ***Special provisions for normal immunoglobulins***

NA

14.11.4 ***Herbal pharmaceutical products***
NA

15. PHARMACEUTICAL FORM
Syrup

16. CLINICAL PARTICULARS

16.1 ***Therapeutic indications***
Loratadine Tablets are indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

16.2 ***Posology and method of administration***
Adults and children over 12 years of age:

10ml (10mg) of the oral solution once daily.

Paediatric population

Children 2 to 12 years of age are dosed by weight:

Body weight more than 30kg: 10ml (10mg) of the oral solution once daily;

Body weight 30kg or less: 5ml (5mg) of the oral solution once daily.

Efficacy and safety of this medicine in children under 2 years of age has not been established.

Patients with hepatic impairment

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An initial dose of 10mg every other day is recommended for adults and children weighing more than 30kg, and for children weighing 30kg or less, 5ml (5mg) every other day is recommended.

Patients with renal impairment

No dosage adjustments are required in the elderly or in patients with renal insufficiency.

16.3 ***Method of administration***
Oral.

16.4 Contraindications
Hypersensitivity to the active substance or to any of the excipients.

16.5 ***Special warnings and precautions for use***
Loratadine Syrup should be administered with caution in patients with severe liver impairment. This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. The administration of Loratadine Tablets should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

16.6 ***Paediatric population***
NA

16.7 ***Interaction with other medicinal products and other forms of interaction***
When administered concomitantly with alcohol, Loratadine Tablets have no potentiating effects as measured by psychomotor performance studies. Potential interaction may occur with all known inhibitors of CYP3A4 or CYP2D6 resulting in elevated levels of Loratadine, which may cause an increase in adverse events. 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).

16.8 ***Additional information on special populations***
NA
16.9 ***Paediatric population***
Interaction studies have only been performed in adults.

16.10 ***Fertility, pregnancy and lactation***
Pregnancy

A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor foeto/ neonatal toxicity of Loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Loratadine during pregnancy.

Breast-feeding

Loratadine is excreted in breast milk, therefore the use of loratadine is not recommended in breast-feeding women.

Fertility

There is no data available on male and female fertility.

16.11 ***Effects on ability to drive and use machines***
In clinical trials that assessed driving ability, no impairment occurred in patients receiving Loratadine. Loratadine tablets has no or negligible influence on the ability to drive and use machines. However, patients should be informed that very rarely some people experienced drowsiness, which may affect their ability to drive or use machines.

16.12 ***Undesirable effects***

Immune system disorders	Very rare	Hypersensitivity reactions (including angioedema and anaphylaxis)
Nervous system disorders	Very rare	Dizziness, convulsion
Cardiac disorders	Very rare	Tachycardia, palpitation
Gastrointestinal disorders	Very rare	Nausea, dry mouth, gastritis
Hepato-biliary disorders	Very rare	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Very rare	Rash, alopecia
General disorders and administration site conditions	Very rare	Fatigue
Investigations	Not known	Weight increased

16.13 ***Overdose***
Overdosage with Loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported with overdoses.

In the event of overdose, 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.

17. PHARMACOLOGICAL PROPERTIES

17.1 *Pharmacodynamic properties*

Pharmacodynamic properties

Mechanism of action

Loratadine, the active ingredient in Loratadine Tablets, is a tricyclic antihistamine with selective, peripheral H_1-receptor activity.

Pharmacodynamic effects

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 H_2-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity. Human histamine skin wheal studies following a single 10 mg dose has shown that the antihistamine effects are seen within 1-3 hours reaching a peak at 8-12 hours and lasting in excess of 24 hours. There was no evidence of tolerance to this effect after 28 days of dosing with Loratadine.

17.2 Pharmacokinetic properties

Absorption

Loratadine is rapidly and well-absorbed. Concomitant ingestion of food can delay slightly the absorption of Loratadine but without influencing the clinical effect. The bioavailability parameters of Loratadine and of the active metabolite are dose proportional.

Distribution

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

In healthy subjects, plasma distribution half-lives of Loratadine and its active metabolite are approximately 1 and 2 hours respectively.

Biotransformation

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 (Tmax) between 1–1.5 hours and 1.5–3.7 hours after administration, respectively.

Elimination

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.

17.3 *Preclinical safety data*

Non-Clinical data reveal no special hazard for humans 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.

17.4 ***Environmental Risk Assessment (ERA)***
NA

18. PHARMACEUTICAL PARTICULARS

18.1 ***List of excipients***
Sucrose BP
Sodium Benzoate BP
Propylene glycol BP
Glycerin BP
Citric acid anhydrous BP
Raspberry berry liquid flavour

18.2 ***Incompatibilities***
NA

18.3 ***Shelf life***
2 Years

18.4 ***Special precautions for storage***
Store in a dry place below 30°C. Protect from light.

18.5 ***Nature and contents of container***
PVC/Alu blister

18.6 ***Special precautions for disposal and other handling***
NA

19. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

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20. MARKETING AUTHORISATION NUMBER: 16934

21. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION: 28/03/2007

22. DATE OF REVISION OF THE TEXT: N/A

23. DOSIMETRY (IF APPLICABLE): N/A

24. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE): N/A

Lorhistina®

1151
Ref. No.:INS151/05.18

Loratadine
Antihistamine

LORHISTINA® TABLETS 10MG
LORHISTINA® SYRUP 5MG/5ML

PRESENTATION:
Lorhistina® Tablets 10mg: White, circular biconvex tablet embossed 'COSMOS' on one side and a breakline on the other side. Each tablet contains: Loratadine 10mg, Lactose and other excipients.
Lorhistina® Syrup 5mg/5mL: Straw yellow coloured syrup slightly viscous free from visible evidence of contamination with raspberry odour. Each 5mL contains: Loratadine 5mg.

CLINICAL PHARMACOLOGY:
Loratadine, a piperidine derivative related to azatadine, is a long-acting, non-sedating antihistamine with no significant antimuscarinic activity.

Pharmacokinetics:
Loratadine is rapidly absorbed from the gastro-intestinal tract after oral administration, peak plasma concentrations being attained in about one hour. Bioavailability is increased and time to peak plasma concentrations is delayed when administered with food. Loratadine undergoes extensive metabolism. The major metabolite, descarboethoxyloratadine (desloratadine), has potent antihistaminic activity. Reported mean elimination half-lives for Loratadine and descarboethoxyloratadine are 8.4 and 28 hours respectively. Loratadine is about 98% bound to plasma proteins; descarboethoxyloratadine is less extensively bound. Loratadine and its metabolites have been detected in the breast milk, but do not appear to cross the blood-brain barrier to a significant extent. Most of a dose is excreted equally in the urine and faeces, mainly in the form of metabolites.

USES:
Lorhistina® is a histamine H_1 - receptor antagonist that does not generally cause sedation or antimuscarinic effect. It is given for symptomatic relief of allergic conditions including rhinitis and chronic urticaria.

DOSAGE AND ADMINISTRATION:
Adults including the elderly and Children 12 years of age and over: 10mg (one tablet) or two 5mL spoonfuls once daily.
Children aged 6 to 12 years: 10mg (one tablet) or two 5mL spoonfuls of syrup once daily.
Children aged 2 to 5 yrs: 5mg (one tablet) or one 5mL spoonful of syrup once daily.

CONTRA-INDICATIONS AND WARNINGS:
Drowsiness can occur and it may affect the performance of skilled tasks. Occasionally reports of convulsions in patients taking antihistamines also call for caution in patients with epilepsy. Caution is also needed in hepatic impairment. Antihistamines should not be given to neonates owing to the increased susceptability to antimuscarinic effects.

Lorhistina®

Adverse Effects:
Occasional gastro-intestinal adverse effects of antihistamines include nausea, vomiting, diarrhoea, or epigastric pain. Administration of antihistamines may sometimes cause rashes and hypersensitivity reaction and cross-sensitivity.
Other adverse effects with antihistamines include convulsions, sweating, myalgia, paraesthesias, extrapyramidal effects, tremor, sleep disturbances, depression, tinnitus, hypotension and hair loss.

Interactions:
Sedative interactions apply to non-sedating antihistamines: they do not appear to potentiate the effects of alcohol, but it should be avoided in excess. Antihistamines may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 25°C. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

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COSMOS

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