1.3 Product Information

1.3.1 Summary Product Characteristics (SPC):

Enclosed

1.3.1 Summary Product Characteristics

1. **Name of product:** ZORACTINE TABLET

Name of the nonproprietary International Product: Loratadine Tablets USP 10 MG

Route of Administration: Oral

2. **Qualitative and Quantitative**

composition: Batch size: 1,00,000 Tablets

Sr. No.	Name of Ingredient	Quantity/ tablet (mg)	Quantity/Batch (Kg)	Functions
Mixing				
1.	Lactose monohydrate BP	64.00	6.4	Diluent
2.	Maize starch BP	23.00	2.3	Diluent
Binding				
3.	Maize Starch BP	7.00	0.700	Binder
4.	Purified water BP*	0.10 ml	10.0 lit	Solvent
Lubrication				
5.	Purified Talc BP	2.00	0.200	Glidant
6.	Magnesium stearate BP	2.00	0.200	Lubricant
7.	Colloidal anhydrous silica BP	2.00	0.200	Lubricant
8.	Loratadine USP	10.00	1.000	H1-antagonist
Total weight of uncoated tablet		**110.00 mg**	**11.000 kg**	

* The materials that will not remain in the final product.

3. **Pharmaceutical Form:** White coloured,, round shaped uncoated tablets having break line on one side of the tablet and plain on the other side

4. Clinical Particulars:

4.1 Therapeutic indications
Loratadine 10mg Tablets is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and method of administration
Adults and children over 12 years of age: 10mg once daily (one tablet once daily). The tablet may be taken without regard to mealtime.

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

Body weight more than 30kg: 10mg once daily (one tablet once daily).

Body weight 30 kg or less: The 10mg strength tablet is not appropriate in children with a body weight less than 30kg.

Efficacy and safety of Loratadine 10 mg Tablets in children under 2 years of age has not been established. The use is therefore not recommended in these patients.

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, 5mg every other day is recommended.

No dosage adjustments are required in older people or in patients with renal insufficiency.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use
Loratadine 10 mg Tablets should be administered with caution in patients with severe liver impairment.

The administration of Loratadine 10 mg Tablets should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

This medicinal products contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
There are no significant interactions between loratadine and food.

When administered concomitantly with alcohol, Loratadine 10 mg Tablets has 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 (see Section 5.2), which may cause an increase in adverse events.

Due to the wide therapeutic index of loratadine no clinically relevant interactions are expected and none were observed in the conducted clinical trials (see Section 5.2).

4.6 Fertility, pregnancy and lactation
Pregnancy

A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor feto/ neonatal toxicity of loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Loratadine 10mg Tablets during pregnancy.

Breast-feeding

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

4.7 Effects on ability to drive and use 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
Summary of the safety profile

In clinical trials involving adults and adolescents in a range of indications including allergic rhinitis (AR) and chronic idiopathic urticaria (CIU), at the recommended dose of 10mg 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%).

Tabulated list of adverse reactions

The following adverse reactions reported during the post-marketing period are listed in the

following table by System Organ Class. Frequencies are defined as 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) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse Experience Term
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
Hepatobiliary 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

Paediatric population

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

4.9 Overdose
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 – H_1 antagonist, ATC code: R06A X13. Loratatine, the active ingredient in Loratadine 10 mg Tablets, is a tricyclic antihistamine with selective, peripheral H_1-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 H_2-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% to 99%) and its active metabolite 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. 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 ingestion of fool 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.

Loratadine and its active metabolite are excreted in the breast milk of lactating women.

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 (120mg) of oral lyophilisates into the hamster cheek pouch for five days.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

1) Maize starch BP
2) Purified water BP
3) Purified Talc BP
4) Magnesium stearate BP
5) Colloidal anhydrous silica BP
6) Lactose monohydrate BP

6.2 Incompatibilities: Not Applicable

6.3 Shelf life: 36 months from the date of manufacturing.

6.4 Special precautions for storage

Do not store above 30°C".
Store in the original package to protect from moisture.

6.5 Nature and contents of container

Product is packed in 10 X 10 Tablets in Alu/PVC Blister pack.

6.6 Special precautions for disposal

No special requirements

6.7 Marketing Authorization Holder:

6.8 Marketing Authorization Number: ---

6.9 Date of first Authorization /renewal of the authorization: ---

6.10 Date of revision of text: ---