PACKAGE INSERT TEMPLATE FOR LORATADINE ORODISPERSIBLE / ORALLY DISINTEGRATING TABLET

Brand or Product Name

[Product name] Orodispersible/Orally Disintegrating Tablet 10mg

Name and Strength of Active Substance(s)

Loratadine 10mg

Product Description

[Visual description of the appearance of the product (eg colour, markings etc)
eg White, circular flat beveled edge tablets marked '100' on one side

Pharmacodynamics

Loratadine is a cyproheptadine, structurally related to azatadine. It exhibits potent, long-acting H_1-antihistamine activity with no central sedative or anticholinergic effects. In man, nasal and other signs and symptoms of allergic rhinitis are relieved rapidly after oral administration.

Loratadine is a tricyclic antihistamine with selective peripheral H_1-receptor antagonistic activity. During studies of its effects on the CNS, loratadine has exhibited no depressant activity and no acute anticholinergic activity.

Loratadine has exhibited a very low affinity for membrane receptors from the cerebral cortex and does not readily penetrate into the CNS. Whole body autoradiographic studies in rats and monkeys, radiolabeled tissue distribution studies in mice and rats, and in vivo radioligand studies in mice have shown that neither loratadine nor its metabolites readily cross the blood-brain barrier. Radioligand binding studies with guinea pig pulmonary and brain H_1-receptors indicate that there was preferential binding to peripheral versus central nervous system H_1-receptors.

The sedation profile of loratadine, 10 mg once daily, is comparable to that of placebo and, 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, does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity.

Pharmacokinetics

After oral administration of loratadine in the conventional tablet formulation, the drug is rapidly and well absorbed and undergoes an extensive first pass metabolism. In normal subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively. Initial data in normal subjects demonstrated a mean elimination half-life of 12.4 hours for loratadine and 19.6 hours for the active metabolite. Subsequent data in normal adult subjects demonstrated mean elimination half-lives of 8.4 hours (range=3 to 20 hours) for loratadine and 28 hours (range=8.8 to 92 hours) for the major active metabolite. In nearly all patients, exposure (AUC) to the metabolite was greater than exposure to the parent compound.

Loratadine is highly bound (97% to 99%) and its active metabolite moderately bound (73% to 76%) to plasma proteins. The bioavailability parameters of loratadine and of the active metabolite are dose proportional. Approximately 40% of the loratadine dose is excreted in the urine and 42% in the feces over a 10-day period and that, mainly in the form of conjugated metabolites. Approximately 27% of the loratadine dose is eliminated in the urine during the first 24 hours. Traces of unchanged loratadine and of its active metabolite were found in the urine.

The pharmacokinetic profile of loratadine and its metabolites is comparable in healthy adult volunteers and in healthy geriatric volunteers. In patients with chronic renal impairment, both the AUCs 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. Hemodialysis 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 of 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. Forty-eight hours after dosing, only 0.029% of the loratadine dose is detected in the milk as unchanged loratadine and its active metabolite.

Pharmacokinetic studies showed that loratadine orodispersible tablet provides plasma concentrations of loratadine and its metabolite, descarboethoxyloratadine, that are similar to those achieved with loratadine in conventional formulations.

The effect of food on the pharmacokinetic profile of loratadine and its metabolite is not regarded as clinically significant. Consumption of food with loratadine orodispersible tablet may delay the time and increase the extent of absorption without influencing clinical effects.

The bioavailability of loratadine or its active metabolite was not compromised when a 10 mg loratadine orodispersible tablet tablet was placed on the tongue and swallowed without water. Loratadine orodispersible tablet may be taken with or without water.

Indication

Loratadine orodispersible tablet is indicated for the relief of symptoms associated with allergic rhinitis, such as sneezing, nasal discharge (rhinorrhea) and itching, as well as ocular itching and burning. Nasal and ocular signs and symptoms are relieved rapidly after oral administration.

Loratadine orodispersible tablet is also indicated for relief of symptoms and signs of chronic urticaria and other allergic dermatologic disorders.

Recommended Dosage

Adults and Children 12 years of age and over

One loratadine orodispersible tablet (10 mg) placed in the mouth once daily. Allow the tablet to disperse in the mouth and swallow. Water or other liquid is not needed.

Before administration, carefully peel off the foil and without crushing the tablet, remove it from the blister pack.

Mode of Administration
Oral

Contraindications

Loratadine orodispersible tablet is contraindicated in patients who have shown hypersensitivity or idiosyncrasy to their components.

Warnings and Precautions

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine; an initial dose of 10 mg (one tablet) every other day is recommended.

[Specific package insert requirement for loratadine]

Warning :

Drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed. The number of subjects who concomitantly received macrolide antibiotics, ketoconazole, cimetidine, ranitidine, or theophylline along with loratadine in controlled clinical trials is too small to rule out possible drug interactions.

Interactions with Other Medicaments

When administered concomitantly with alcohol, loratadine has no potentiating effects as measured by psychomotor performance studies.

Loratadine is metabolised by hepatic cytochromes P450 3A4 and 2D6. Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin or cimetidine in controlled clinical trials, but without clinically significant changes (including electrocardiographic). Other drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed. Other drugs known to inhibit either P450 3A4 or P450 2D6 are quinidine, fluconazole or fluoxetine.

Loratadine orodispersible tablet may be administered without regard to meals.

Drug/Laboratory Test Interactions

Loratadine orodispersible tablet should be discontinued 48 hours prior to skin testing procedures since antihistamines may prevent or diminish otherwise positive reactions to dermal reactivity indicators.

Statement on Usage During Pregnancy and Lactation

Safe use of loratadine orodispersible tablet during pregnancy has not been established; therefore, use only if potential benefit justifies potential risk to fetus.

Since loratadine is excreted in breast milk and because of the increased risk of antihistamines for infants, particularly newborns and premature infants, a decision should be made whether to discontinue nursing or discontinue the drug.

Adverse Effects / Undesirable Effects

Loratadine orodispersible tablet were well tolerated and did not cause local irritation or taste abnormalities. Overall, the incidence of adverse reactions was comparable to that of placebo.

The most frequently reported adverse effect was headache. Rarely reported undesirable effects included somnolence, fatigue, dry mouth, dyspepsia, epistaxis and pharyngitis.

During the marketing of loratadine in conventional formulations, alopecia, anaphylaxis, and abnormal hepatic function have been reported rarely.

Overdose and Treatment

Somnolence, tachycardia and headache have been reported with overdoses of the conventional loratadine formulation. A single dose of 160 mg caused no significant side effects.

If necessary, the treatment of overdosage is symptomatic. Adsorption of any drugs remaining in the stomach may be attempted by the administration of activated charcoal as a slurry with water, gastric lavage should be considered. Physiologic saline solution is the lavage solution of choice, particularly in children. In adults, tap water can be used; however, as much as possible of the amount administered should be removed before the next instillation. Saline cathartics draw water into the bowel by osmosis and, therefore, may be valuable for their action in rapid dilution of bowel content. Loratadine is not cleared by hemodialysis to any appreciable extent. After emergency treatment, the patient should continue to be medically monitored.

Storage Conditions
Store below ….°C

Dosage Forms and Packaging Available
[Packaging type & pack size eg Alu-alu blister of 10s X 10/box, HDPE bottle of 30s/box etc]

Name and Address of Manufacturer
[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder
[Name & full address of marketing authorization holder]

Date of Revision of Package Insert

Updated August 2011

[day/month/year]