Allereze

Loratadine

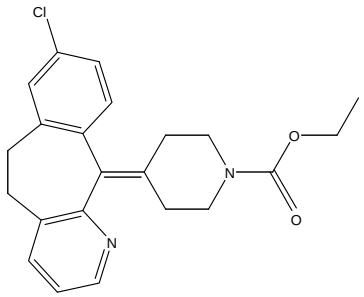
PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredient: Loratadine.

Chemical name: ethyl 4-(8-chloro-5,6-dihydro-11H-benzo 5,6-cyclohepta 1,2-b pyridin-11-ylidene)-1-piperidinecarboxylate.

Structural formula:



Molecular formula: $C_{22}H_{23}N_2ClO_2$

Molecular weight: 382.9

CAS Registry no.: 79794-75-5

DESCRIPTION

Loratadine is freely soluble in methanol, ethanol and chloroform, soluble in ether and practically insoluble in water.

Each Allereze tablet contains loratadine 10 mg as the active ingredient. The inactive excipients are: lactose, cellulose - microcrystalline, starch - maize, starch - pregelatinised maize, silicon dioxide, magnesium stearate, carnauba wax, talc- purified and Opadry Clear YS-1R-7006.

PHARMACOLOGY

Loratadine is a potent, long acting antihistamine with relative selectivity for peripheral histamine H_1-receptors. Loratadine does not readily penetrate into the CNS. It exhibits greater affinity for peripheral H_1-receptors than for central H_1-receptors. These properties account for the observed lack of sedation. The incidence of sedation with loratadine is comparable to that of placebo.

Loratadine has a rapid onset of action after oral administration, usually within one hour.

Specific studies involving sleep tests with EEG tracings, motor car driving under actual driving conditions as well as psychomotor performance tests have not shown any significant difference between loratadine 10 mg and placebo with respect to interaction with the CNS or impairment of performance.

Specific clinical pharmacology studies were conducted with concomitant administration of loratadine with therapeutic doses of erythromycin, ketoconazole, and cimetidine for 10 days in healthy subjects. Although increased plasma concentrations ($AUC_{0\text{-}24hrs}$) of loratadine and/or its active metabolite descarboethoxyloratadine (desloratadine) were observed, there were no clinically relevant changes in the safety profile of loratadine as assessed by electrocardiographic parameters including QT_c interval, clinical laboratory tests, vital signs and adverse events. Additionally, cardiac repolarisation was not altered, nor were other electrocardiographic parameters (see **PRECAUTIONS - Interactions with Other Medicines)**.

Pharmacokinetics

Loratadine is well absorbed with peak plasma levels occurring at approximately one or two hours after dosing. The drug is almost totally metabolised. It has an active metabolite desloratadine.

In man, loratadine is extensively bound to plasma protein (97 to 99%) and desloratadine, moderately bound (73 to 76%).

Approximately 40% of the dose is excreted in the urine and 42% in the faeces in a 10-day period. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. The mean elimination half-life of loratadine in normal volunteers is approximately 12 hours while that of desloratadine is approximately 20 hours. Renal impairment has no significant effect on loratadine clearance. In children, clearance appears to be marginally faster. Concomitant ingestion of food with loratadine may delay absorption (by approximately one hour) and may increase the AUC for both loratadine (40%) and its active metabolite desloratadine (approximately 15%). These differences would not be expected to be clinically important.

INDICATIONS

In adults and children 12 years +and older, Allereze tablets are indicated for the:

- treatment of seasonal and perennial allergic rhinitis
- relief of symptoms and signs of chronic urticaria.

CONTRAINDICATIONS

Allereze tablets are contraindicated in patients who have shown hypersensitivity or idiosyncrasy to loratadine, desloratadine or any of the excipients.

PRECAUTIONS

Immune system. In a 17-month study in monkeys, loratadine demonstrated no functional impairment of the immune system as indicated by mortality, peripheral leucocyte count or incidences of inflammatory reactions, autoimmune disease and malignancy. Specific studies investigating the effect of loratadine on immune function in man have not been performed.

Hepatic. As with all drugs metabolised by the liver, loratadine should be used with caution in patients with severe liver dysfunction.

Carcinogenesis. Loratadine administered in the diet to mice for 18 months at doses greater than 12 mg/kg/day resulted in an increased incidence of benign hepatic tumours. A 2-year study in rats showed no increase in the incidence of carcinogenicity in loratadine-treated animals compared with control animals at dietary doses up to 25 mg/kg/day.

Fertility. Animal studies showed that loratadine had an adverse effect on male fertility when administered to rats at doses greater than 24 mg/kg/day. The clinical relevance of this observation is unknown at this time.

Use in Pregnancy (Category B1)

Reproductive studies in pregnant rats and rabbits showed no evidence of embryotoxic or teratogenic activity at loratadine doses up 96 mg/kg/day. In pregnant rats, loratadine and its metabolite crossed the placental barrier, distributing in foetal tissues in a pattern similar to that in maternal tissues but at lower concentrations.

The safe use of loratadine during pregnancy has not been established. Therefore, the compound should be used only if the potential benefit justifies the potential risk to the foetus.

Australian categorisation definition of Category B1: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Use in Lactation

The safe use of loratadine during lactation has not been established. Therefore, the use of loratadine by breastfeeding mothers is not recommended. The compound should be used only if the potential benefit justifies the potential risk to the infant.

A study in lactating women showed that breast milk levels of loratadine and its active metabolite parallel their respective plasma concentrations after oral administration. Acute toxicity studies have demonstrated that neonatal rats and mice are more sensitive to loratadine than the adults of the corresponding species.

Interactions with Other Medicines

Various tests (psychomotor tests, wakefulness tests, cognitive function and mood tests and driving tests) have shown that loratadine does not interact with alcohol.

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

Loratadine (10 mg once daily) has been safely co-administered with therapeutic doses of erythromycin, cimetidine and ketoconazole in controlled clinical pharmacology studies. Although increased plasma concentrations ($AUC_{0\text{-}24hrs}$) of loratadine and/or descarboethoxyloratadine were observed following coadministration of loratadine with each of these drugs in normal volunteers, there were no clinically relevant changes in the safety profile of loratadine and no reports of sedation or syncope (see **Pharmacology** section).

Effects on Laboratory Tests

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

ADVERSE EFFECTS

In worldwide controlled clinical studies, the incidence of adverse effects associated with loratadine has been comparable to that of placebo. In these trials, loratadine has shown no clinically significant sedative or anticholinergic properties.

Most commonly reported side effects for loratadine include headache (12% vs placebo 11%), sedation (8% vs placebo 6%), fatigue (4% vs placebo 3%) and dry mouth (3% vs placebo 2%).

Adverse experiences occurring in less than 1% of patients are listed below.

Cardiovascular. Hypertension, hypotension, syncope, palpitation, tachycardia, chest pain, epistaxis.

Gastrointestinal. Dyspepsia, diarrhoea, constipation, abdominal/gastric pain, nausea.

Renal. Increased frequency of urination, urine discolouration.

Respiratory. Nasal dryness, pharyngitis, coughing.

Other. Depression, dizziness, fever, nervousness, viral infection, insomnia, menstruation delay, myalgia, pruritus, altered taste, paroniria, tinnitus, rash on face, increased saliva, increased appetite, paraesthesia, malaise and alopecia.

The incidence and general nature of these rarer reports were similar in both placebo-treated and loratadine-treated patients.

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

DOSAGE AND ADMINISTRATION

Adults and children 12 years of age and over. 10 mg (one tablet) daily.

For patients with severe hepatic impairment a lower initial dose (5 mg daily) is recommended.

OVERDOSAGE

Somnolence, tachycardia and headache have been reported with overdoses. In volunteer studies, single doses of up to 160 mg have been administered without any untoward effects.

In the event of overdosage, consideration should be given to adsorption of any unabsorbed loratadine by use of activated charcoal. Otherwise, treatment, which should be started immediately, is symptomatic and supportive. Loratadine is not eliminated by haemodialysis; it is not known if loratadine is eliminated by peritoneal dialysis. After emergency treatment, the patient should continue to be medically monitored.

For further information in the case of overdose or suspected overdose, contact the Poisons Information Centre on 13 11 26.

PRESENTATION AND STORAGE CONDITIONS

Allereze Loratadine 10 mg film-coated tablets: white, round, biconvex, scored on one side and marked "LR" over "10" on the reverse; blister packs of 10, 30, 50, 70* and 90* tablets.

* Not marketed in Australia.

Store below 25°C.

POISON SCHEDULE OF THE MEDICINE

S2 - Pharmacy Medicine

NAME AND ADDRESS OF THE SPONSOR

Alphapharm Pty Limited

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

ABN 93 002 359 739

www.alphapharm.com.au

DATE OF APPROVAL

Approved by the Therapeutic Goods Administration on 15 March 2005.

Date of most recent amendment: 21 October 2010.