Aeriallerg
Desloratadine

Description:
Each Aeriallerg tablet contains 5.0mg of desloratadine.

Actions:
Desloratadine is a non-sedating long-acting hitamine antagonist with potent, selective peripheral H_1-receptor antagonist activity. Desloratadine has demonstrated antiallergic, antihistaminic, and anti-inflammatory activity.

Preclinical Toxicology:
Desloratadine is the primary active metabolite of loratadine. Preclinical studies conducted with desloratadine and loratadine demonstrated that there are no qualitative or quantitative differences in the toxicity profile of desloratadine and loratadine at comparable levels of exposure to desloratadine.

Preclinical data with desloratadine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction. The lack of carcinogenic potential was demonstrated in studies conducted with loratadine.

Clinical Pharmacology
Pharmacodynamic Properties:
After oral administration, desloratadine selectively blocks peripheral histamine H_1-recptors because the drug is effectively excluded from entry to the central nervous system (CNS).

In addition to antihistaminic activity, desloratadine has demonstrated antiallergic and anti-inflammatory activity from numerous *in vitro* (mainly conducted on cells of human origin) and *in vivo* studies. These studies have shown that desloratadine inhibits the broad cascade of events that initiate and propagate allergic inflammation, including,

- the release of proinflammatory cytokines including IL-4, IL-6, IL-8, IL-13.
- the release of important proinflammatory chemokines such as RANTES (Regulated upon Activation, Normal T-cell Expressed and Secreted),
- superoxide anion production by activated polymorphonuclear neutrophils,
- eosinophil adhesion and chemotaxis,
- the expression of the adhesion molecules such as P-selectin,

- lgE-dependent release of histamine, prostaglandin (PGD2), and leukortriene (LTC4),
- the acute allergic bronchoconstrictor response and allergic cough in animal models.

In a multiple dose clinical trial, in which up to 20mg of desloratadine was administered daily for 14 days, no statistically or clinically relevant cardiovascular effect was observed. In a clinical pharmacologic trial, in which desloratadine was administered at a dose of 45mg daily (nine times the clinical dose) for ten days, no prolongation of the QTc interval was seen.

Desloratadine does not readily penetrate the central nervous system. At the recommended dose of 5mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine tablets even at a dose of 7.5mg daily did not affect psychomotor performance in clinical trials. A single dose of desloratadine 5mg did not affect standard measures of flight performance including exacerbation of subjective sleepiness or tasks related to flying.

No clinically relevant changes in desloratadine plasma concentrations were observed in multiple-dose ketoconazole, erythromycin, azithromycin, fluoxetine and cimetidine interaction trials.

In clinical pharmacologic trials, co-administration of alcohol did not increase the alcohol-induced impairment in performance or increase in sleepiness. No significant differences were found in the psychomotor test results between desloratadine and placebo groups, whether administered alone or with alcohol.

In patients with allergic rhinitis (AR), Desloratadine was effective in relieving symptoms such as sneezing, nasal discharge and itching, congestion/stuffing, as well as ocular itching, tearing and redness, and itching of palate. Desloratadine effectively controlled symptoms for 24 hours.

In two 4-weeks trials in patients with seasonal allergic rhinitis (SAR) and concurrent asthma, desloratadine was shown to be effective in reducing the symptoms of SAR (rhinorrhea, nasal congestion, nasal itching and sneezing, itching/burning eyes, tearing/watering eyes, redness of eyes, and itching of ears or palate) and asthma (coughing, wheezing, difficulty breathing), and decreasing beta-agonist use. FEV_1 was not altered in the desloratadine or placebo treatment groups.

In trials conducted in patients with chronic idiopathic urticaria (CIU), desloratadine was effective in relieving pruritus and decreasing the size and number of hives as early as 1 day after initiation of treatment. In each trial, the

effects were sustained over the 24 hour dosing interval. Treatment with desloratadine tablets also improved sleep and daytime function, as measured by reduced interference with sleep and routine daily activities.

Desloratadine was effective in alleviating the burden of seasonal allergic rhinitis as shown by the total score of the rhino-conjunctivitis quality of life questionnaire. The greatest amelioration was seen in the domains of practical problems and daily activities limited by symptoms.

Pharmacokinetic Properties:
Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine administration. Desloratadine is well absorbed with maximum concentration achieved after approximately 3 hours; the terminal phase half-life is approximately 27 hours. The degree of accumulation of desloratadine was consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. The bioavailability of desloratadine was dose proportional over the range of 5mg to 20mg.

Desloratadine is moderately bound (83%-87%) to plasma proteins. There is no evidence of clinically relevant drug accumulation following once daily dosing of desloratadine (5mg to 20mg) for 14 days.

The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore some interactions with other drugs can not be fully excluded. *In-vivo* studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that these enzymes are not important in the metabolism of desloratadine. Desloratadine does not inhibit CYP3A4 or CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

In a single dose trial using a 7.5mg dose of desloratadine, there was no effect of food (high-fat, high caloric breakfast) on the disposition of desloratadine. In another study, grapefruit juice had no effect on the disposition of desloratadine.

Indications and Usage:
Aeriallerg is indicated for the rapid relief of symptoms associated with allergic rhinitis, such as sneezing, nasal discharge and itching, congestion/stuffiness, as well as ocular itching, tearing and redness, itching of palate and coughing.

Aeriallerg is also indicated for the relief of symptoms associated with chronic idiopathic urticaria such as the relief of itching and the size and number of hives.

Dosage and Administration:
Adults and adolescents (≥ 12 years of age): One Aeriallerg 5mg film-coated tablet once a day regardless of mealtime. For oral use.

Drug Interactions:
No clinically relevant interactions with desloratadine was observed in clinical trials.

There was no effect of food or grapefruit juice on the disposition of desloratadine.

Desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol.

Adverse Effects:
In clinical trials in a range of indications including allergic rhinitis and idiopathic Uticria, at the recommended dose of 5mg daily, undesirable effects with desloratadine was reported in 3% of patients in excess of those treated with placebo. The most frequent adverse events reported in excess of placebo were fatigue (1.2%), dry mouth (0.8%), and headache (0.6%).

Very rare cases of hypersensitivity reactions (including anaphylaxis and rash) tachycardia, palpitations, psychomotor hyperactivity, seizures, elevations of liver enzymes, hepatitis, and increased bilirubin have been reported during the marketing of desloratadine.

Contraindications:
Hypersensitivity to the active substance or to any of excipients or to loratadine.

Precautions:
Efficacy and safety of desloratadine in children under 12 years of age have not been established.

Effects on ability to drive and use machines:
No effects on the ability to drive and use machines have been observed.

Usage during pregnancy and lactation:
No overall effect on rat fertility was observed with desloratadine at an exposure that was 34 times higher than the exposure in humans at the recommended clinical dose.

No teratogenic or mutagenic effects were observed in animal trials with desloratadine. Since no clinical data on exposed pregnancies are available with desloratadine, the safe use of desloratadine during pregnancy has not been established. Desloratadine is not to be used during pregnancy unless the potential benefits outweigh the risks.

Desloratadine is excreted into breast milk, therefore the use of desloratadine is not recommended in breast-feeding women.

Overdosage Information:
In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.

Based on a multiple dose clinical trial in adults and adolescents, in which up to 45mg of desloratadine was administered (9 times the clinical dose), no clinically relevant effects were observed.

Desloratadine is not eliminated by hemodialysis; it is not known if it is eliminated by peritoneal dialysis.

Presentation:
Aeriallerg 5mg available in packs of 30 tabs.

Storage Conditions:
Store between 2º and 30ºC.