RINAZAL

Tablets & Syrup

Composition

Rinazal Syrup

Each 5 ml contains Desloratadine 2.5 mg

Action

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

Pharmacodynamics

After oral administration, Desloratadine selectively blocks peripheral histamine H_1-receptors because the drug is effectively excluded from entry to the central nervous system.

In addition to antihistaminic activity, Desloratadine has demonstrated antiallergic and anti-inflammatory activities 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,
- IgE-dependent release of histamine, prostaglandin (PGD2), and leukotriene (LTC4),
- The acute allergic bronchoconstrictor response and allergic cough in animal models.

Desloratadine does not readily penetrate the central nervous system. No clinically relevant changes in Desloratadine plasma concentrations were observed in multiple-dose azithromycin, fluoxetine, cimetidine, ketoconazole and erythromycin.

Co-administration of alcohol did not increase the alcohol-induced impairment in performance or increase in sleepiness. A single dose of Desloratadine 5 mg did not affect standard measures of flight performance including exacerbation of subjective sleepiness or tasks related to flying.

Assessments of quality of life in the clinical trials indicated that seasonal allergic rhinitis produced a consistent burden of disease, and that improvements in therapeutic responses were associated with improvements in various quality of life domains including vitality and social functioning.

Pharmacokinetics

Absorption

Desloratadine plasma concentrations can be detected within 30 minutes of Desloratadine administration in adults and adolescents. 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 5 mg to 20 mg.

Distribution

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

Biotransformation

The enzyme responsible for the metabolism of Desloratadine has not been identified yet, and therefore, some interactions with other medicinal products cannot be fully excluded. Desloratadine does not inhibit CYP3A4 *in vivo,* and *in vitro* studies have shown that the medicinal product does not inhibit CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

Elimination
In a single dose trial using a 7.5 mg 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.

Renally impaired patients
The pharmacokinetics of Desloratadine in patients with chronic renal insufficiency (CRI) was compared with that of healthy subjects in one single-dose study and one multiple dose study. In the single-dose study, the exposure to Desloratadine was approximately 2 and 2.5-fold greater in subjects with mild to moderate and severe CRI, respectively, than in healthy subjects. In the multiple-dose study, steady state was reached after Day 11, and compared to healthy subjects the exposure to Desloratadine was ~1.5-fold greater in subjects with mild to moderate CRI and ~2.5-fold greater in subjects with severe CRI. In both studies, changes in exposure (AUC and C_{max}) of Desloratadine and 3-hydroxydesloratadine were not clinically relevant.

Indications
- Rinazal is indicated for the relief of symptoms associated with seasonal and perennial allergic rhinitis, such as sneezing, nasal discharge and itching, congestion/stuffiness, as well as ocular itching, tearing and redness, itching of palate and coughing.
- Rinazal 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.

Contraindications
Hypersensitivity or idiosyncrasy to Desloratadine, or to Loratadine.

Warnings and Precautions
Efficacy and safety of Desloratadine in children under 6 months of age have not been established. Although Desloratadine is unlikely to affect the ability to drive or operate machinery, a few people may be affected and care should be taken.

Pregnancy
CategoryC
Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers
Desloratadine passes into breast milk. Hence, the use of Desloratadine by breastfeeding mothers is not recommended.

Adverse Reactions
Desloratadine Syrup
The most frequent adverse events reported were diarrhea (3.7%), fever (2.3%) and insomnia (2.3%).

Desloratadine Tablets
The most frequent adverse events reported were fatigue (1.2%), dry mouth (0.8%), and headache (0.6%).

Post Marketing
The following spontaneous adverse events have been reported during the marketing of Desloratadine: tachycardia, palpitations and rarely hypersensitivity reactions (such as rash, pruritus,

urticaria, edema, dyspnea, and anaphylaxis), and elevated liver enzymes including bilirubin and very rarely hepatitis

Drug Interactions

No clinically relevant interactions with Desloratadine were observed in clinical trials. Desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol. There was no effect of food or grapefruit juice on the disposition of Desloratadine.

Laboratory Interactions

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

Dosage and Administration

Rinazal can be taken regardless of mealtime.

- Adults and adolescents 12 years and over: One Rinazal 5mg film-coated tablet or 10 ml (5 mg) Rinazal Syrup once daily.
- Children 6 to 11 years of age: 5 ml (2.5 mg) Rinazal Syrup once daily.
- Children 2 to 5 years of age: 2.5 ml (1.25 mg) Rinazal Syrup once daily.
- Children 6 to 11 months of age: 2 ml (1 mg) of Rinazal Syrup once daily.

Over dosage

In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.
Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis.

Storage

Tablets: store below 30°C. Protect from moisture.
Syrup: store below 30° C. Store in original container.

Presentation

Rinazal Syrup
Bottle of 120 ml