

DATA SHEET

AERIUS TABLETS AND SYRUP

NAME OF MEDICINE

AERIUS (desloratadine 5 mg) Tablets
AERIUS (desloratadine 0.5 mg/mL) Syrup

DESCRIPTION

AERIUS tablets contain desloratadine 5 mg and the following inactive ingredients:

Core: calcium hydrogen phosphate, microcrystalline cellulose, maize starch and talc

Coating: Opadry Blue, Opadry Clear, carnauba wax and white beeswax

AERIUS Syrup contains desloratadine 0.5 mg/mL and the following inactive ingredients:

Propylene glycol, sorbitol, anhydrous citric acid, sodium citrate, disodium edetate, sucrose, bubble gum flavour, colour E110, water and sodium benzoate as preservative.

USES

Actions

Desloratadine is a non-sedating long-acting histamine antagonist with potent, selective peripheral H₁-receptor antagonist activity. Desloratadine has demonstrated antiallergic, antihistaminic and anti-inflammatory activities.

Pharmacodynamics

After oral administration, desloratadine selectively blocks peripheral histamine H₁-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.

In a multiple dose clinical trial, in which up to 20 mg of desloratadine was administered daily for 14 days, no statistically or clinically relevant cardiovascular effect was observed. In a clinical pharmacological trial, in which desloratadine was administered at a dose of 45 mg 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. AERIUS at a dose of 7.5 mg daily did not affect psychomotor performance in clinical trials.

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

In clinical pharmacological 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.

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.

In addition to the established classifications of seasonal and perennial, allergic rhinitis can alternatively be classified as intermittent and persistent allergic rhinitis according to the duration of symptoms. Intermittent allergic rhinitis is defined as the presence of symptoms for less than 4 days per week or for less than 4 weeks. Persistent allergic rhinitis is defined as the presence of symptoms for 4 days or more per week and for more than 4 weeks.

Preclinical Safety

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.

Pharmacokinetics

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 5 mg to 20 mg.

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.

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

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 a single dose, crossover trial of desloratadine, the tablet and syrup formulations were bioequivalent and not affected by the presence of food (high fat, high caloric breakfast).

In another study, grapefruit juice had no effect on the disposition of desloratadine.

In separate single dose studies, at the recommended doses, paediatric patients had comparable AUC and C_{max} values of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Clinical Studies

Seasonal Allergic Rhinitis

In adult and adolescent patients with seasonal allergic rhinitis, AERIUS tablets were effective in relieving symptoms such as sneezing, nasal discharge and itching, congestion/stuffiness, as well as ocular itching, tearing and redness, and itching of palate. AERIUS tablets effectively controlled symptoms for 24 hours.

AERIUS 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.

In two 4-week trials in adults and adolescents with seasonal allergic rhinitis and concurrent asthma, desloratadine was shown to be effective in reducing the symptoms of seasonal allergic rhinitis (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. FEV₁ was not altered in the desloratadine or placebo treatment groups.

Chronic Idiopathic Urticaria

In trials conducted in adults and adolescents with chronic idiopathic urticaria, AERIUS tablets were 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 AERIUS tablets also improved sleep and daytime function, as measured by reduced interference with sleep and routine daily activities.

Paediatric Population

Safety of AERIUS Syrup was demonstrated in three paediatric trials. Children aged 6 months -11 years who were candidates for antihistamine therapy received a daily dose of AERIUS 1 mg (6 to 11 months of age), AERIUS 1.25 mg (1 to 5 years of age) or AERIUS 2.5 mg (6 to 11 years of age). Treatment was well tolerated as documented by clinical laboratory tests, vital signs and ECG interval data, including QTc. When given at the recommended doses, the plasma concentration of desloratadine was comparable in the paediatric and adult populations. Although the efficacy of desloratadine has not been demonstrated in children under the age of 2 years, the course of the diseases (seasonal and perennial allergic rhinitis and chronic idiopathic urticaria) and the pharmacokinetic profile of desloratadine are similar in adults and paediatric patients. Therefore, desloratadine efficacy data in adults can be extrapolated to the paediatric population.

INDICATIONS

AERIUS 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.

AERIUS 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

AERIUS can be taken regardless of mealtime for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and chronic idiopathic urticaria.

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or for less than 4 weeks) should be managed in accordance with the evaluation of the patient's disease history and the treatment should be discontinued after symptoms are resolved and reinitiated upon their reappearance. In persistent allergic rhinitis (presence of symptoms for 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during allergen exposure periods.

Adults and adolescents 12 years and over: One AERIUS 5mg film-coated tablet or 10 mL (5 mg) AERIUS Syrup once daily.

Children 6 to 11 years of age: 5 mL (2.5 mg) AERIUS Syrup once daily.

Children 2 to 5 years of age: 2.5 mL (1.25 mg) AERIUS Syrup once daily.

Children 6 to 11 months of age: 2 mL (1 mg) of AERIUS Syrup once daily.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Efficacy and safety of AERIUS in children under 6 months of age have not been established.

Although AERIUS is unlikely to affect the ability to drive or operate machinery, a few people may be affected and care should be taken.

Use in Pregnancy (Category B1)

The safe use of desloratadine during pregnancy has not been established. Therefore, AERIUS is not to be used during pregnancy unless clearly indicated.

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.

Use in Lactation

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

Carcinogenicity and Mutagenicity

Desloratadine has no carcinogenic risk in man based on the available data with loratadine. Desloratadine showed no mutagenic effects in *in vitro* and *in vivo* mutagenicity studies.

Drug Interactions

No clinically relevant interactions with AERIUS were observed in clinical trials (see **Pharmacology** section).

AERIUS 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

AERIUS 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 REACTIONS

In clinical trials in a paediatric population, AERIUS Syrup was administered to a total of 246 children aged 6 months to 11 years. The overall incidence of adverse events in children 2 to 11 years of age was similar for AERIUS syrup and placebo groups. In infants and toddlers aged 6 to 23 months, the most frequent adverse events reported in excess of placebo were diarrhoea (3.7%), fever (2.3%) and insomnia (2.3%).

In clinical trials in a range of indications including seasonal allergic rhinitis and chronic idiopathic urticaria, at the recommended dose of 5 mg daily, undesirable effects with AERIUS Tablets were 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%).

No effects on the ability to drive and use machines have been observed with the use of desloratadine.

Very rare cases of hypersensitivity reactions (including anaphylaxis and rash), psychomotor hyperactivity and seizures have been reported during the marketing of desloratadine.

In addition, cases of tachycardia, palpitations, elevations of liver enzymes, hepatitis, and increased bilirubin have been reported very rarely.

In clinical trials in a paediatric population, AERIUS syrup was administered to 115 children ages 2 through 11 years. The overall incidence of adverse events was similar for the AERIUS Syrup and the placebo groups.

OVERDOSAGE

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 45 mg of desloratadine was administered (9 times the clinical dose), no clinically relevant effects were observed.

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

PHARMACEUTICAL PRECAUTIONS

Tablets: The shelf-life is 24 months when stored below 25°C. Protect from moisture.

Syrup: The shelf-life is 24 months when stored below 30°C. Store in original container.

MEDICINE CLASSIFICATION

Pharmacy Medicine

PRESENTATION AND PACKAGE QUANTITIES

Tablets:	5 mg, light blue round embossed film coated	-	10s, 30s
Syrup:	0.5 mg/mL, clear orange coloured solution	-	100 mL and 200 mL

NAME AND ADDRESS

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