SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Aerius tablets 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg of desloratadine.
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of symptoms associated with allergic rhinitis such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate. For relief of symptoms associated with urticaria such as itching and rash.

4.2 Posology and Method of Administration

For relief of symptoms associated with allergic rhinitis (including intermittent and persistent) and urticaria, Aerius® is taken with or without meal.
Adults and adolescents (12 years of age and over) take one tablet (5 mg) once a day.
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 patient's disease history. 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 the allergen exposure periods.
Pediatric population
There is limited clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age.
The safety and efficacy of Aerius 5 mg tablets in children below the age of 12 years have not been established. No data are available.
Additional information for special populations
Geriatric population:
The safety and efficacy of Aerius® has not been established for geriatric population.
Renal impairment:
Aerius® should be used with caution in patients with severe renal failure.
Hepatic impairment:
There is no data regarding administration of Aerius® in patients with hepatic impairment.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients or to loratadine.

4.4 Special Warnings and Precautions for Use

Efficacy and safety of Aerius® tablets in children under 12 years of age have not been established (a tablet cannot be divided into equal parts, and the tablet dose is

indicated for children of 12 years and more). Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children, being more susceptible to develop new seizures under desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions with Other Medicinal Products and Other Forms of Interactions

In multiple joint application of desloratadine with ketoconazole, erythromycin, azithromycin, fluoxetine, cimetidine clinically significant changes of desloratadine concentration in plasma were not detected.
In a clinical pharmacology trial, Aerius tablets taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol. However, cases of alcohol intolerance and intoxication have been reported during post-marketing use. Therefore, caution is recommended if alcohol is taken concomitantly.
Pediatric population: interaction studies have only been performed in adults.

4.6 Pregnancy and Lactation

A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicate no malformative nor foeto/ neonatal toxicity of desloratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Aerius® during pregnancy.
Desloratadine is excreted into breast milk, therefore the use of Aerius® is not recommended in breastfeeding women.

4.7 Effects on Ability to Drive and Use Machinery

Aerius has no or negligible influence on the ability to drive and use machines based on clinical trials. Patients should be informed that most people do not experience drowsiness. Nevertheless, as there is individual variation in response to all medicinal products, it is recommended that patients are advised not to engage in activities requiring mental alertness, such as driving a car or using machines, until they have established their own response to the medicinal product.

4.8 Undesirable Effects

In clinical trials in a range of indications including 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 of adverse events reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %).
Pediatric population
In a clinical trial with 578 adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this occurred in 5.9 % of patients treated with desloratadine and 6.9 % of patients receiving placebo.
Tabulated list of adverse reactions
The frequency of the clinical trial adverse reactions reported in excess of placebo and other undesirable effects reported during the post-marketing period are listed in the following table.

Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reactions seen with Aerius
Psychiatric disorders	Very rare Not known	Hallucinations Abnormal behavior, aggression
Nervous system disorders	Common Very rare	Headache Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Very rare Not known	Tachycardia, palpitations QT prolongation
Gastrointestinal disorders	Common Very rare	Dry mouth Abdominal pain, nausea, vomiting, dyspepsia, diarrhea
Hepatobiliary disorders	Very rare Not known	Elevations of liver enzymes, increased bilirubin, hepatitis Jaundice
Skin and subcutaneous tissue disorders	Not known	Photosensitivity
Musculoskeletal and connective tissue disorders	Very rare	Myalgia
General disorders and administration site conditions	Common Very rare Not known	Fatigue Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnea, pruritus, rash, and urticaria) Asthenia

Pediatric population
Other undesirable effects reported during the post-marketing period in pediatric patients with an unknown frequency included QT prolongation, arrhythmia, bradycardia, abnormal behavior, and aggression.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

The adverse event profile associated with overdosage, as seen during post-marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic treatment is recommended.

Based on clinical trials in adults and adolescents, in which up to 45 mg of desloratadine was administered (nine times the recommended dose), no clinically relevant effects were observed. Desloratadine is not eliminated by hemodialysis; it is not known if it is eliminated by peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

ATC code: R06AX27.
Pharmacotherapeutic group: antihistamines for systemic use.

5.1 Pharmacodynamic Properties

Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H_1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H_1- receptors because the substance is excluded from entry to the central nervous system.

Desloratadine has demonstrated antiallergic properties from *in vitro* studies. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.

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 pharmacology trial, in which desloratadine was administered at a dose of 45 mg daily (nine times the clinical dose) for ten days, no prolongation of QTc interval was seen.

No clinically relevant changes in desloratadine plasma concentrations were ketoconazole and erythromycin interaction trials.

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

In clinical pharmacology trials, co-administration with 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, Aerius® was effective in relieving symptoms such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate. Aerius® effectively controlled symptoms for 24 hours. The efficacy of Aerius® tablets has not been clearly demonstrated in trials with adolescent patients 12 through 17 years of age.

In addition to the established classifications of seasonal and perennial, allergic rhinitis can alternatively be classified as intermittent allergic rhinitis 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.

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

Chronic idiopathic urticaria was studied as a clinical model for urticarial conditions, since the underlying pathophysiology is similar, regardless of etiology, and because chronic patients can be more easily recruited prospectively. Since histamine release is a causal factor in all urticarial diseases, desloratadine is expected to be effective in providing symptomatic relief for other urticaria conditions, in addition to chronic idiopathic urticaria, as advised in clinical guidelines.

In two placebo-controlled six-week trials in patients with chronic idiopathic urticaria, Aerius® was effective in relieving pruritus and decreasing the size and number of hives by the end of the first dosing interval. In each trial, the effects were sustained over the 24 hour dosing interval. As with other antihistamine trials in chronic idiopathic urticaria, the minority *of* patients who were identified as non-responsive to antihistamines was excluded. An improvement in pruritus of more than 50 % was observed in 55 % of patients treated with desloratadine compared with 19 % of patients treated with placebo. Treatment with Aerius® also significantly reduced interference with sleep and daytime function, as measured by a four-point scale used to assess these variables.

5.2 Pharmacokinetic Properties

Desloratadine plasma concentrations can be detected within 30 minutes of administration. Maximum concentration of desloratadine is achieved after approximately 3 hours; the half-life is approximately 27 hours. The degree of accumulation of desloratadine was consistent with its half-life (approximately 27 hours) and dosing frequency. The bioavailability of desloratadine was dose proportional over the range of 5 mg to 20 mg.

In a pharmacokinetic trial in which patient demographics were comparable to those of the general seasonal allergic rhinitis population, 4 % of the subjects achieved a higher concentration of desloratadine. This percentage may vary according to ethnic background. Maximum desloratadine concentration was about 3-fold higher at approximately 7 hours with *a* terminal phase half-life of approximately 89 hours. The safety profile of these subjects was not different from that of the general population.

Desloratadine is moderately bound (83 % - 87 %) to plasma proteins. There is no evidence of clinically relevant medicine accumulation following once daily dosing of desloratadine (5 mg to 20 mg) for 14 days. The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore, some interactions with other medicinal products can not 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.

In a single dose trial using a 7.5 mg dose *of* desloratadine, there was no effect of food (high-fat, high caloric breakfast) or grapefruit juice 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Calcium hydrogen phosphate dihydrate
Cellulose, microcrystalline
Maize starch
Talc
Lactose monohydrate
Hydroxypropyl methylcellulose
Titanium dioxide
Polyethylene glycol
FD&C blue No.2 aluminium lake
Carnauba wax
White beeswax

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years. Do not use after the expiration date shown on the package.

6.4 Special Precautions for Storage

Do not store above 30 ºC. Keep out of reach of children.

6.5 Nature and Contents of Container

Tablets 5 mg #7, #10 in blisters are placed in a carton.

6.6 Rules for dispensing in pharmacies

Medicinal product subject to medical prescription

7. MAH NAME AND ADDRESS

JSC “BAYER”,
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