

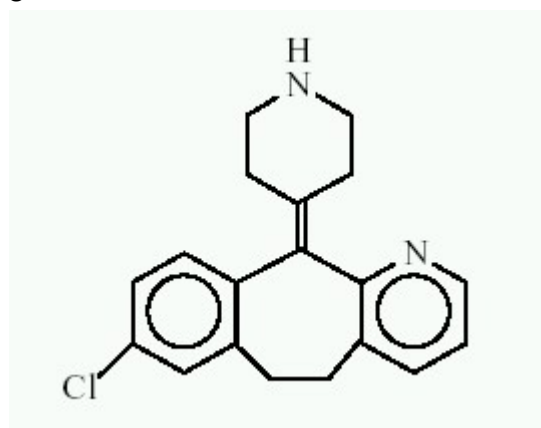
# AERIUS<sup>®</sup>

Desloratadine

FILM COATED TABLETS

**DESCRIPTION:** AERIUS (desloratadine) Film coated Tablets are light blue, round, film coated tablets containing 5 mg desloratadine, an antihistamine, to be administered orally. It also contains the following excipients: dibasic calcium phosphate dihydrate USP, microcrystalline cellulose NF, corn starch NF, talc USP, carnauba wax NF, white wax NF, coating material consisting of lactose monohydrate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and FD&C Blue # 2 Aluminum Lake.

Desloratadine is a white to off-white powder that is slightly soluble in water, but very soluble in ethanol and propylene glycol. It has an empirical formula:  $C_{19}H_{19}ClN_2$  and a molecular weight of 310.8. The chemical name is 8-chloro-6,11-dihydro-11-(4-piperdinylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine and has the following structure :



## CLINICAL PHARMACOLOGY:

**Mechanism of Action:** Desloratadine is a longacting tricyclic histamine antagonist with selective H<sub>1</sub>-receptor histamine antagonist activity. Receptor binding data indicates that at a concentration of 2 – 3 ng/mL (7 nanomolar),

desloratadine shows significant interaction with the human histamine H<sub>1</sub>-receptor. Desloratadine inhibited histamine release from human mast cells *in vitro*.

Results of a radiolabeled tissue distribution study in rats and a radioligand H<sub>1</sub>-receptor binding study in guinea pigs showed that desloratadine did not readily cross the blood brain barrier. The clinical significance of this finding is unknown.

**Pharmacokinetics: Absorption:** Following oral administration of desloratadine 5 mg once daily for 10 days to normal healthy volunteers, the mean time to maximum plasma concentrations ( $T_{max}$ ) occurred at approximately 3 hours post dose and mean steady state peak plasma concentrations ( $C_{max}$ ) and area under the concentration-time curve (AUC) of 4 ng/mL and 56.9 ng·hr/mL were observed, respectively. Neither food nor grapefruit juice had an effect on the bioavailability ( $C_{max}$  and AUC) of desloratadine.

**Distribution:** Desloratadine and 3-hydroxydesloratadine are approximately 82% to 87% and 85% to 89%, bound to plasma proteins, respectively. Protein binding of desloratadine and 3-hydroxydesloratadine was unaltered in subjects with impaired renal function.

**Metabolism:** Desloratadine (a major metabolite of loratadine) is extensively metabolized to 3-hydroxydesloratadine, an active metabolite, which is subsequently glucuronidated. The enzyme(s) responsible for the formation of 3-hydroxydesloratadine have not been identified. Data from clinical trials indicate that a subset of the general patient population has a decreased ability to form 3-hydroxydesloratadine, and are slow metabolizers of desloratadine. In pharmacokinetic studies (n=3748), approximately 6% of subjects were slow metabolizers of desloratadine (defined as a subject with an AUC ratio of 3-hydroxydesloratadine to desloratadine less than 0.1, or a subject with a desloratadine half-life exceeding 50 hours). The frequency of slow metabolizers is higher in Blacks (17%, n=990) as compared to Caucasians (2%, n=1,460) and Hispanics (2%, n=1,063). The median exposure (AUC) to desloratadine in the slow metabolizers was approximately 6-fold greater than the subjects who are not slow metabolizers. Subjects who are slow metabolizers of desloratadine cannot be prospectively identified and will be

exposed to higher levels of desloratadine following dosing with the recommended dose of desloratadine. Although not seen in these pharmacokinetic studies, patients who are slow metabolizers may be more susceptible to dose-related adverse events.

**Elimination:** The mean elimination half-life of desloratadine was 27 hours.

$C_{max}$  and AUC values increased in a dose proportional manner following single oral doses between 5 and 20 mg. The degree of accumulation after 14 days of dosing was consistent with the half-life and dosing frequency. A human mass balance study documented a recovery of approximately 87% of the  $^{14}C$ -desloratadine dose, which was equally distributed in urine and feces as metabolic products. Analysis of plasma 3-hydroxydesloratadine showed similar  $T_{max}$  and half-life values compared to desloratadine.

**Special Populations: Geriatric:** In older subjects ( $\geq 65$  years old;  $n=17$ ) following multiple-dose administration of AERIUS Tablets, the mean  $C_{max}$  and AUC values for desloratadine were 20% greater than in younger subjects ( $<65$  years old). The oral total body clearance (CL/F) when normalized for body weight was similar between the two age groups. The mean plasma elimination half-life of desloratadine was 33.7 hr in subjects  $\geq 65$  years old. The pharmacokinetics for 3-hydroxydesloratadine appeared unchanged in older versus younger subjects. These age-related differences are unlikely to be clinically relevant and no dosage adjustment is recommended in elderly subjects.

**Renally Impaired:** Desloratadine pharmacokinetics following a single dose of 7.5 mg were characterized in patients with mild ( $n=7$ ; creatinine clearance 51-69 mL/min/1.73  $m^2$ ), moderate ( $n=6$ ; creatinine clearance 34-43 mL/min/1.73  $m^2$ ), and severe ( $n=6$ ; creatinine clearance 5-29 mL/min/1.73  $m^2$ ) renal impairment or hemodialysis dependent ( $n=6$ ) patients. In patients with mild and moderate renal impairment, median  $C_{max}$  and AUC values increased by approximately 1.2- and 1.9-fold, respectively, relative to subjects with normal renal function. In patients with severe renal impairment or who were hemodialysis dependent,  $C_{max}$  and AUC values increased by approximately 1.7- and 2.5-fold, respectively. Minimal changes in 3-hydroxydesloratadine

concentrations were observed. Desloratadine and 3-hydroxydesloratadine were poorly removed by hemodialysis. Plasma protein binding of desloratadine and 3-hydroxydesloratadine was unaltered by renal impairment. Dosage adjustment for patients with renal impairment is recommended (see **DOSAGE AND ADMINISTRATION** section).

**Hepatically Impaired:** Desloratadine pharmacokinetics were characterized following a single oral dose in patients with mild (n=4), moderate (n=4), and severe (n=4) hepatic impairment as defined by the Child-Pugh classification of hepatic function and 8 subjects with normal hepatic function. Patients with hepatic impairment, regardless of severity, had approximately a 2.4-fold increase in AUC as compared with normal subjects. The apparent oral clearance of desloratadine in patients with mild, moderate, and severe hepatic impairment was 37%, 36%, and 28% of that in normal subjects, respectively. An increase in the mean elimination half-life of desloratadine in patients with hepatic impairment was observed. For 3-hydroxydesloratadine, the mean  $C_{max}$  and AUC values for patients with hepatic impairment were not statistically significantly different from subjects with normal hepatic function. Dosage adjustment for patients with hepatic impairment is recommended (see **DOSAGE AND ADMINISTRATION** section).

**Gender:** Female subjects treated for 14 days with AERIUS Tablets had 10% and 3% higher desloratadine  $C_{max}$  and AUC values, respectively, compared with male subjects. The 3-hydroxydesloratadine  $C_{max}$  and AUC values were also increased by 45% and 48%, respectively, in females compared with males.

However, these apparent differences are not likely to be clinically relevant and therefore no dosage adjustment is recommended.

**Race:** Following 14 days of treatment with AERIUS Tablets, the  $C_{max}$  and AUC values for desloratadine were 18% and 32% higher, respectively in Blacks compared with Caucasians. For 3-hydroxydesloratadine there was a corresponding 10% reduction in  $C_{max}$  and AUC values in Blacks compared to Caucasians. These differences are not likely to be clinically relevant and therefore no dose adjustment is recommended.

**Drug Interactions:** In two controlled crossover clinical pharmacology studies in healthy male (n=12 in each study) and female (n=12 in each study) volunteers, desloratadine 7.5 mg (1.5 times the daily dose) once daily was coadministered with erythromycin 500 mg every 8 hours or ketoconazole 200 mg every 12 hours for 10 days. In 3 separate controlled, parallel group clinical pharmacology studies, desloratadine at the clinical dose of 5 mg has been coadministered with azithromycin 500 mg followed by 250 mg once daily for 4 days (n=18) or with fluoxetine 20 mg once daily for 7 days after a 23 day pretreatment period with fluoxetine (n=18) or with cimetidine 600 mg every 12 hours for 14 days (n=18) under steady state conditions to normal healthy male and female volunteers. Although increased plasma concentrations ( $C_{max}$  and  $AUC_{0-24\text{ hrs}}$ ) of desloratadine and 3-hydroxydesloratadine were observed (see Table 1), there were no clinically relevant changes in the safety profile of desloratadine, as assessed by electrocardiographic parameters (including the corrected QT interval), clinical laboratory tests, vital signs, and adverse events.

**Table 1**

Changes in Desloratadine and 3-Hydroxydesloratadine Pharmacokinetics in Healthy Male and Female Volunteers

	<u>Desloratadine</u>		<u>3-Hydroxydesloratadine</u>	
	$C_{max}$	$AUC_{0-24hrs}$	$C_{max}$	$AUC_{0-24hrs}$
<b>Erythromycin</b> (500 mg Q8h)	+ 24%	+ 14%	+ 43%	+ 40%
<b>Ketoconazole</b> (200 mg Q12h)	+ 45%	+ 39%	+ 43%	+ 72%
<b>Azithromycin</b> (500 mg day 1, 250 mg QD x 4 days)	+ 15%	+ 5%	+ 15%	+ 4%
<b>Fluoxetine</b> (20 mg QD)	+ 15%	+ 0%	+ 17%	+ 13%
<b>Cimetidine</b> (600 mg Q12h)	+ 12%	+ 19%	- 11%	- 3%

**Pharmacodynamics:**

**Wheal and Flare:** Human histamine skin wheal studies following single and repeated 5 mg doses of desloratadine have shown that the drug exhibits an antihistaminic effect by 1 hour; this activity may persist for as long as 24 hours. There was no evidence of histamine-induced skin wheal tachyphylaxis within the desloratadine 5 mg group over the 28 day treatment period.

The clinical relevance of histamine wheal skin testing is unknown.

**Effects on QTc:** Single daily doses of 45 mg were given to normal male and female volunteers for 10 days. All ECGs obtained in this study were manually read in a blinded fashion by a cardiologist. In AERIUS-treated subjects, there was an increase in mean heart rate of 9.2 bpm relative to placebo. The QT interval was corrected for heart rate (QT<sub>c</sub>) by both the Bazett and Fridericia methods. Using the QT<sub>c</sub> (Bazett) there was a mean increase of 8.1 msec in AERIUS-treated subjects relative to placebo. Using QT<sub>c</sub> (Fridericia) there was a mean increase of 0.4 msec in AERIUS-treated subjects relative to placebo. No clinically relevant adverse events were reported.

#### **Clinical Trials:**

**Seasonal Allergic Rhinitis:** The clinical efficacy and safety of AERIUS Tablets were evaluated in over 2,300 patients 12 to 75 years of age with seasonal allergic rhinitis. A total of 1,838 patients received 2.5 – 20 mg/day of AERIUS in 4 double-blind, randomized, placebo-controlled clinical trials of 2- to 4-weeks duration conducted in the United States. The results of these studies demonstrated the efficacy and safety of AERIUS 5 mg in the treatment of adult and adolescent patients with seasonal allergic rhinitis. In a dose ranging trial, AERIUS 2.5-20 mg/day was studied. Doses of 5, 7.5, 10, and 20 mg/day were superior to placebo; and no additional benefit was seen at doses above 5.0 mg. In the same study, an increase in the incidence of somnolence was observed at doses of 10 mg/day and 20 mg/day (5.2% and 7.6%, respectively), compared to placebo (2.3 %).

In 2 four-week studies of 924 patients (aged 15 to 75 years) with seasonal allergic rhinitis and concomitant asthma, AERIUS Tablets 5 mg once daily improved rhinitis symptoms, with no decrease in pulmonary function. This

supports the safety of administering AERIUS Tablets to adult patients with seasonal allergic rhinitis with mild to moderate asthma.

AERIUS Tablets 5 mg once daily significantly reduced the Total Symptom Scores (the sum of individual scores of nasal and non-nasal symptoms) in patients with seasonal allergic rhinitis. See Table 2.

**Table 2**  
TOTAL SYMPTOM SCORE (TSS)  
Changes in a 2 Week Clinical  
Trial in Patients with Seasonal Allergic Rhinitis

Treatment Group (n)	Mean Baseline* (SEM)	Change from Baseline** (SEM)	Placebo Comparison (P- value)
AERIUS 5.0 mg (171)	14.2 (0.3)	-4.3 (0.3)	P=<0.01
Placebo (173)	13.7 (0.3)	-2.5 (0.3)	
SEM = Standard Error of the Mean *At baseline, a total nasal symptom score (sum of 4 individual symptoms) of at least 6 and a total non-nasal symptom score (sum of 4 individual symptoms) of at least 5 (each symptom scored 0 to 3 where 0=no symptom and 3=severe symptoms) was required for trial eligibility. TSS ranges from 0=no symptoms to 24=maximal symptoms. **Mean reduction in TSS averaged over the 2-week treatment period.			

There were no significant differences in the effectiveness of AERIUS Tablets 5 mg across subgroups of patients defined by gender, age, or race.

**Perennial Allergic Rhinitis:** The clinical efficacy and safety of AERIUS Tablets 5 mg were evaluated in over 1,300 patients 12 to 80 years of age with perennial allergic rhinitis. A total of 685 patients received 5 mg/day of AERIUS in 2 double blind, randomized, placebo controlled clinical trials of 4 weeks duration conducted in the United States and internationally. In one of these

studies AERIUS Tablets 5 mg once daily was shown to significantly reduce symptoms of perennial allergic rhinitis (**Table 3**).

**Table 3**  
TOTAL SYMPTOM SCORE (TSS)  
Changes in a 4 Week Clinical  
Trial in Patients with Perennial Allergic Rhinitis

Treatment Group (n)	Mean Baseline* (SEM)	Change from Baseline** (SEM)	Placebo Comparison (P- value)
AERIUS 5.0 mg (337)	12.37 (0.18)	-4.06 (0.21)	P=0.01
Placebo (337)	12.30 (0.18)	-3.27 (0.21)	
SEM = Standard Error of the Mean *At baseline, average of total symptom score (sum of 5 individual nasal symptoms and 3 non-nasal symptoms, each symptom scored 0 to 3 where 0=no symptom and 3=severe symptoms) of at least 10 was required for trial eligibility. TSS ranges from 0=no symptoms to 24=maximal symptoms. **Mean reduction in TSS averaged over the 4-week treatment period.			

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.

#### **Chronic Idiopathic Urticaria:**

The efficacy and safety of AERIUS Tablets 5 mg once daily was studied in 416 chronic idiopathic urticaria patients 12 to 84 years of age, of whom 211 received AERIUS. In two double-blind, placebo-controlled, randomized clinical



trials of six weeks duration, at the pre-specified one-week primary time point evaluation, AERIUS Tablets significantly reduced the severity of pruritus when compared to placebo (**Table 4**). Secondary endpoints were also evaluated and during the first week of therapy AERIUS Tablets 5 mg reduced the secondary endpoints, “Number of Hives” and the “Size of the Largest Hive”, when compared to placebo

**Table 4**  
**PRURITUS SYMPTOM SCORE**  
 Changes in the First Week of a Clinical  
 Trial in Patients with Chronic Idiopathic Urticaria

Treatment Group (n)	Mean Baseline (SEM)	Change from Baseline* (SEM)	Placebo Comparison (P- value)
AERIUS 5.0 mg (115)	2.19 (0.04)	-1.05 (0.07)	P<0.01
Placebo (110)	2.21 (0.04)	-0.52 (0.07)	
Pruritus scored 0 to 3 where 0 = no symptom to 3 = maximal symptom SEM = Standard Error of the Mean *Mean reduction in pruritus averaged over the first week of treatment.			

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 urticarial conditions, in addition to chronic idiopathic urticaria, as advised in clinical guidelines.

#### INDICATIONS AND USAGE:

**Allergic Rhinitis:** AERIUS Tablets 5 mg are indicated for the relief of the nasal and non-nasal symptoms of allergic rhinitis (including intermittent and persistent allergic rhinitis) in patients 12 years of age and older.

**Urticaria:** AERIUS Tablets are indicated for the symptomatic relief of pruritus, reduction in the number of hives, and size of hives, in patients with urticaria 12 years of age and older.

**DOSAGE AND ADMINISTRATION:** In adults and children 12 years of age and over; the recommended dose of AERIUS Tablets is 5 mg once daily. In patients with liver or renal impairment, a starting dose of one 5 mg tablet every other day is recommended based on pharmacokinetic data.

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 and the treatment could 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.

**CONTRAINDICATIONS:** AERIUS Tablets 5 mg are contraindicated in patients who are hypersensitive to this medication or to any of its ingredients, or to loratadine.

#### **PRECAUTIONS:**

##### **Carcinogenesis, Mutagenesis, Impairment of Fertility:**

##### **Carcinogenicity Studies**

The carcinogenic potential of desloratadine was assessed using a loratadine study in rats and a desloratadine study in mice. In a 2-year study in rats, loratadine was administered in the diet at doses up to 25 mg/kg/day (approximately 45 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD). A significantly higher incidence of hepatocellular tumors (combined adenomas and carcinomas) was observed in males given 10 mg/kg/day of loratadine (approximately 10 times the summed AUC-based exposure of desloratadine and its metabolite at the

RHD) and in males and females given 25 mg/kg/day of loratadine. The clinical significance of these findings during long-term use of desloratadine is not known. In a 2-year dietary study in mice, males and females given up to 16 mg/kg/day and 32 mg/kg/day desloratadine, respectively (approximately 30 and 70 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD, respectively), did not show significant increases in the incidence of any tumors.

### **Genotoxicity Studies**

In genotoxicity studies with desloratadine, there was no evidence of genotoxic potential in a reverse mutation assay (*Salmonella/E. coli* mammalian microsome bacterial mutagenicity assay) or in two assays for chromosomal aberrations (human peripheral blood lymphocyte clastogenicity assay and mouse bone marrow micronucleus assay).

### **Impairment of Fertility**

In a female fertility study, desloratadine was given to female rats orally 14 days prior to and throughout mating until Gestation Day 7 at doses of 6, 12 and 24 mg/kg/day. An increase in preimplantation loss and a decrease in number of implantations and fetuses noted at 24 mg/kg (approximately 200 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD) was likely due to maternal toxicities including reduced body weight gain and food consumption. In a male fertility study in rats, desloratadine was given orally to male rats for 70 days prior to mating and throughout the mating period (total dosing period 106-108 days) at doses of 3, 12 and 40 mg/kg/day. Reduced body weight gain, food consumption, and absolute organ weights of testes, epididymis, and cauda epididymis were noted at 40 mg/kg/day. A male-specific decrease in fertility, demonstrated by reduced female conception rates, decreased sperm numbers and motility, and histopathologic changes in testes and epididymis, occurred at a dose of 12 mg/kg or greater (approximately 65 times or greater than the summed AUC-based exposure of desloratadine and its metabolite at the RHD). Desloratadine had no effect on male fertility in rats at 3 mg/kg/day (approximately 10 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD).

### **Pregnancy**

#### Risk Summary

The limited available data with CLARINEX in pregnant women are not sufficient to inform a drug-associated risk for major birth defects and miscarriage. There are no adequate and well-controlled studies in pregnant women. Desloratadine given during organogenesis to pregnant rats was not teratogenic at the summed area under the concentration-time curve (AUC)-based exposures of desloratadine and its metabolite approximately 320 times that at the recommended human daily oral dose (RHD) of 5 mg/day. Desloratadine given during organogenesis to pregnant rabbits was not teratogenic at the AUC-based exposures of desloratadine approximately 230 times that at the RHD. Desloratadine given to pregnant rats during organogenesis through lactation resulted in reduced body weight and slow righting reflex of F1 pups at the summed AUC-based exposures of desloratadine and its metabolite approximately 70 times or greater than that at the RHD.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 24% and 15-20%, respectively.

#### Data

##### *Animal Data*

Desloratadine was given orally during organogenesis to pregnant rats at doses of 6, 24 and 48 mg/kg/day (approximately 50, 200 and 320 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD). No fetal malformations were present. Reduced fetal weights and skeletal variations noted at doses of 24 and 48 mg/kg/day were likely secondary to the maternal toxicities of reduced body weight gain and food consumption observed at the same doses. Desloratadine was also given orally during organogenesis to pregnant rabbits at doses of 15, 30 and 60 mg/kg/day (approximately 30, 70 and 230 times the AUC-based exposure of desloratadine at the RHD). No adverse effects to the fetus were noted. Reduced maternal body weight gain was noted in rabbits at 60 mg/kg/day. In a peri-and post-natal development study, desloratadine was given to rats orally during the perinatal (Gestation Day 6) through lactation periods (Postpartum Day 21) at doses of 3, 9 and 18 mg/kg/day. Reduced body weight and slow righting reflex were reported in F1 pups at doses of 9 mg/kg/day or greater (approximately 70 times or greater than the summed AUC-based exposure of desloratadine and its metabolite at the RHD). Desloratadine had no effect on F1 pup development at 3 mg/kg/day (approximately 10 times the summed AUC-based exposure of desloratadine and its metabolite at the RHD). Maternal toxicities including reduced body weight gain and food consumption

were noted at 18 mg/kg/day for F0 dams. F1 offspring were subsequently mated and there was no developmental toxicity for F2 pups observed.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, desloratadine should be used during pregnancy only if clearly needed.

**Nursing Mothers:** Desloratadine passes into breast milk, therefore a decision should be made whether to discontinue nursing or to discontinue desloratadine, taking into account the importance of the drug to the mother.

**Pediatric Use:** The safety and effectiveness of AERIUS Tablets in pediatric patients under 12 years of age have not been established.

**Geriatric Use:** Clinical studies of desloratadine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. (see **CLINICAL PHARMACOLOGY- Special Populations**).

**Information for Patients:** Patients should be instructed to use AERIUS Tablets as directed. As there are no food effects on bioavailability, patients can be instructed that AERIUS Tablets may be taken without regard to meals. Patients should be advised not to increase the dose or dosing frequency as studies have not demonstrated increased effectiveness at higher doses and somnolence may occur.

Desloratadine should be administered with caution in patients with a medical or family history of seizures. In particular, young children may be more susceptible to developing new seizures under desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

## **ADVERSE REACTIONS:**

**Allergic Rhinitis:** In multiple-dose placebo-controlled trials, 2,834 patients ages 12 years or older received AERIUS Tablets at doses of 2.5 mg to 20 mg daily, of whom 1,655 patients received the recommended daily dose of 5 mg. In patients receiving 5 mg daily, the rate of adverse events was similar between AERIUS and placebo-treated patients. The percent of patients who withdrew prematurely due to adverse events was 2.4% in the AERIUS group and 2.6% in the placebo group. There were no serious adverse events in these trials in patients receiving desloratadine. All adverse events that were reported by greater than or equal to 2% of patients who received the recommended daily dose of AERIUS Tablets (5.0 mg once-daily), and that were more common with AERIUS Tablet than placebo, are listed in Table 5.

**Table 5**  
**Incidence of Adverse Events Reported by  $\geq 2\%$  of Adults and Adolescent Allergic Rhinitis Patients Receiving AERIUS Tablets**

Adverse Event	AERIUS Tablets 5 mg (n=1655)	Placebo (n=1652)
<b><i>Infections and Infestations</i></b>	4.1%	2.0%
<i>Pharyngitis</i>		
<b><i>Nervous System Disorders</i></b>	2.1%	1.8%
<i>Somnolence</i>		
<b><i>Gastrointestinal Disorders</i></b>	3.0%	1.9%
<i>Dry Mouth</i>		
<b><i>Musculoskeletal System and Breast Disorders</i></b>	2.1%	1.8%
<i>Myalgia</i>		
<b><i>Reproductive System and Breast Disorders</i></b>	2.1%	1.6%
<i>Dysmenorrhea</i>		
<b><i>General Disorders and Administration Site Conditions</i></b>	2.1%	1.2%
<i>Fatigue</i>		

The frequency and magnitude of laboratory and electrocardiographic abnormalities were similar in AERIUS and placebo-treated patients.

There were no differences in adverse events for subgroups of patients as defined by gender, age, or race.

**Chronic Idiopathic Urticaria:** In multiple-dose, placebo-controlled trials of chronic idiopathic urticaria, 211 patients ages 12 years or older received AERIUS Tablets and 205 received placebo. Adverse events that were reported by greater than or equal to 2% of patients who received AERIUS Tablets and that were more common with AERIUS than placebo were (rates for AERIUS and placebo, respectively):

headache (14%, 13%), nausea (5%, 2%), fatigue (5%, 1%), dizziness (4%, 3%), pharyngitis (3%, 2%), dyspepsia (3%, 1%), and myalgia (3%, 1%).

The following spontaneous adverse events have been reported during the marketing of desloratadine: tachycardia, and rarely hypersensitivity reactions (such as rash, pruritus, urticaria, edema, dyspnea, and anaphylaxis), psychomotor hyperactivity, somnolence, seizures, hepatitis, elevated liver enzymes including bilirubin and increased appetite.

**DRUG ABUSE AND DEPENDENCE:** There is no information to indicate that abuse or dependency occurs with AERIUS Tablets.

**OVERDOSAGE:** In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Desloratadine and 3-hydroxydesloratadine are not eliminated by hemodialysis.

Information regarding acute overdosage is limited to experience from post-marketing adverse event reports and from clinical trials conducted during the development of the AERIUS product. In a dose-ranging trial, at doses of 10 mg and 20 mg/day somnolence was reported.

In another study, no clinically relevant adverse events were reported in normal male and female volunteers who were given single daily doses of AERIUS 45

mg for 10 days. All ECGs obtained in this study were manually read in a blinded fashion by a cardiologist. In AERIUS-treated subjects, there was an increase in mean heart rate of 9.2 bpm relative to placebo. The QT interval was corrected for heart rate (QT<sub>c</sub>) by both the Bazett and Fridericia methods. Using the QT<sub>c</sub> (Bazett) there was a mean increase of 8.1 msec in AERIUS-treated subjects relative to placebo. Using QT<sub>c</sub> (Fridericia) there was a mean increase of 0.4 msec in AERIUS-treated subjects relative to placebo. No clinically relevant adverse events were reported.

#### **PRESENTATIONS:**

AERIUS Tablet, box of 2 blisters of 15 film-coated tablets.

Reg.No: DKI0887101417A1

#### **STORAGE:**

Store below 30° C. Protect from excessive moisture.

#### **ON MEDICAL PRESCRIPTION ONLY HARUS DENGAN RESEP DOKTER**

Manufactured by :

Schering-Plough Labo N.V., Belgium

Registered by :

PT Organon Pharma Indonesia Tbk

Pasuruan, Jawa Timur

#### **References:**

PI 07/08 LRN: 034117-DL-TB-PIPB.3

S-CCDS-MK4117-MTL-112014

S-CCDS-MK4117-MTL-042017

S-CCDS-MK4117-MTL-112017 ver.2.0

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