Technical Specifications
Packaging Machine: IMA

size:	180x420mm
fold:	180x35mm
carton weight:	50gsm
standard number of colors	1

designed by: Pantoula Irene

Date modified: *20/12/2012*

Version: 2

Approved by:

printable area

Front Page

50mm

60mm

30mm

Ajalorin Orodispersible Tablet 2.5 mg
Ajalorin Orodispersible Tablet 5 mg

4th folding

Strength
Each orodispersible tablet contains Desloratadine 2.5mg.
Each orodispersible tablet contains Desloratadine 5mg.

Product Description
2.5mg: Red-brick, round, flat tablets with bevel edges and embossed with '2.5'.
5mg: Red-brick, round, flat tablets with bevel edges and embossed with '5'.

Pharmacodynamics
Pharmacotherapeutic group: antihistamines - H1 antagonist

ATC-code:
R606A X27

3rd folding

pharmacode
reading direction

Mechanism of action
Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H1-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.

Clinical efficacy and Safety
In a multiple dose clinical trial, desloratadine orodispersible tablets were well tolerated. At the recommended dose, desloratadine 5mg orodispersible tablet was found to be bioequivalent to the 5mg conventional tablet formulation of desloratadine. Therefore, the efficacy of desloratadine orodispersible tablet is expected to be the same as with the desloratadine tablet formulation.

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 observed in multiple-dose ketoconazole and erythromycin interaction trials.

Desloratadine does not readily penetrate the central nervous system. In clinical trials, at the recommended dose of 5 mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine tablets given at a single daily dose of 7.5 mg did not affect psychomotor performance in clinical trials. 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.

2nd folding

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, desloratadine tablets was effective in relieving symptoms such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate. Desloratadine tablets effectively controlled symptoms for 24 hours.

Paediatric population
The efficacy of desloratadine tablets have 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.

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.

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.

In two placebo-controlled six week trials in patients with chronic idiopathic urticaria, desloratadine 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 nonresponsive 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 desloratadine also significantly reduced interference with sleep and daytime function, as measured by a four-point scale used to assess these variables.

Pharmacokinetics
Absorption
Desloratadine plasma concentrations can be detected within 30 minutes of 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.

In a series of pharmacokinetic and clinical trials, 6 % of the subjects reached a higher concentration of desloratadine. The prevalence of this poor metaboliser phenotype was comparable for adult (6 %) and paediatric subjects 2- to 11-year old (6 %), and greater among Blacks (18 % adult, 16 % paediatric) than Caucasians (2 % adult, 3 % paediatric) in both populations however the safety profile of these subjects was not different from that of the general population.

In a multiple-dose pharmacokinetic study conducted with the tablet formulation in healthy adult subjects, four subjects were found to be poor metabolisers of desloratadine. These subjects had a Cmax concentration about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours.

Distribution
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.

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.

1st folding

In single-dose crossover studies of desloratadine 5 mg orodispersible tablets with desloratadine 5mg conventional tablets or desloratadine 5mg oral lyophilisate, the formulations were bioequivalent.

Desloratadine 2.5mg tablets has not been evaluated in paediatric patients however in conjunction with the dose finding studies in paediatrics, the pharmacokinetics data for desloratadine orodispersible tablets supports the use of the 2.5 mg dose in paediatric patients 6 to 11 years of age.

Elimination
The presence of food prolongs Tmax for desloratadine from 2.5 to 4 hours and Tmax for 3-OH-desloratadine from 4 to 6 hours. In a separate study, grapefruit juice had no effect on the disposition of desloratadine. Water had no effect on the bioavailability of desloratadine orodispersible tablets.

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 Cmax) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

Pre-clinical Safety Data
Desloratadine is the primary active metabolite of loratadine. Non-clinical 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.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. The collective analysis of preclinical and clinical irritation studies for the orodispersible tablet indicate that this formulation in unlikely to pose risk for local irritation with clinical use. The lack of carcinogenic potential was demonstrated in studies conducted with desloratadine and loratadine.

Indication
Ajalorin 2.5mg Orodispersible Tablets are indicated in adults, adolescents aged 12 years and older and children aged 6-11 years old for the relief of symptoms associated with:
- allergic rhinitis
- urticaria

Ajalorin 5mg Orodispersible Tablets are indicated in adults, adolescents aged 12 years and older for the relief of symptoms associated with:
- allergic rhinitis
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Recommended Dosage
Ajalorin 2.5mg Orodispersible Tablet
Adults and adolescents 12 years of age and over
The recommended dose of Desloratadine 2.5mg orodispersible tablets is two 2.5mg orodispersible tablets placed in the mouth once a day.

Paediatric population
Children 6 to 11 years of age: the recommended dose of desloratadine is one 2.5 mg orodispersible tablet placed in mouth once a day.

The safety and efficacy of desloratadine 2.5mg orodispersible tablets in children below the age of 6 years have not been established. No data are available.

There is limited clinical trial efficacy experience with the use of desloratadine in children 6 through 11 years of age.

There is limited clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age.

Back Page

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 the allergen exposure periods.

Ajalorin 5mg Orodispersible Tablet
Adults and adolescents 12 years of age and over
The recommended dose of Desloratadine 5mg orodispersible tablet is one 5mg orodispersible tablets placed in the mouth 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 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 the allergen exposure periods.

Paediatric 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 desloratadine 5mg orodispersible tablets in children below the age of 12 years have not been established. No data are available.

Method of Administration
Oral use
The dose can be taken with or without food. Immediately before use, the blister must be carefully peeled open and the dose of orodispersible tablet removed without crushing it. The dose of orodispersible tablet is placed in the mouth where it will disperse immediately. Water or other liquid is not needed to swallow the dose. The dose must be taken as soon as the blister has been opened.

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

Warnings and Precautions
In the case of severe renal insufficiency, Ajalorin orodispersible tablets should be used with caution (see section pharmacokinetic).

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.

This product contains aspartame. It may be harmful for people with phenylketonuria.

Interactions with Other Medicaments
No clinically relevant interactions were observed in clinical trials with desloratadine tablets in which erythromycin or ketoconazole were co-administered (see section pharmacodynamic).

Paediatric population
Interaction studies have only been performed in adults.

In a clinical pharmacology trial, desloratadine 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.

Pregnancy and Lactation:
Pregnancy
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 (see section preclinical safety data). As a precautionary measure, it is preferable to avoid the use of desloratadine during pregnancy.

Breastfeeding
Desloratadine has been identified in breastfed newborns/infants of treated women. The effect of desloratadine on newborns/infants is unknown. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from desloratadine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
There are no data available on male and female fertility.

Adverse Effects/ Undesirable Effects:
Summary of the safety profile

Paediatric population
In clinical trials in a paediatric population, the desloratadine syrup formulation was administered to a total of 246 children aged 6 months through 11 years. The overall incidence of adverse events in children 2 through 11 years of age was similar for the desloratadine and the placebo groups. In infants and toddlers aged 6 to 23 months, the most frequent advers reactions reported in excess of placebo were diarrhea (3.7%), fever (2.3%) and insomnia (2.3%). In an additional study, no adverse events were seen in subjects between 6 and 11 years of age following a single 2.5mg dose of desloratadine oral solution.

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.

Adults and adolescents
At the recommended dose, in clinical trials involving adults and adolescents in a range of indications including allergic rhinitis and chronic idiopathic urticarial, undesirable effects with desloratadine 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%).

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 (≥ 1/1000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (<1/10,000) not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reactions seen with Desloratadine.
Psyciatric disorders	Very rare	Hallucinations
	Not known	Abnormal Behaviour, aggression
Nervous system disorders	Common	Headache
	Common (Children less than 2 years)	Insomnia
	Very rare	Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Very rare	Tachycardia
	Not known	QT prolongation
Gastrointestinal disorders	Common	Dry mouth
	Common (children less than 2 years)	Diarrhoea
	Very rare	Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea
Hepatobiliary disorders	Very rare	Elevations of liver enzymes, increased bilirubin, hepatitis
	Not known	Jaundice
Skin and subcutaneous tissue disorder	Not known	Photosensitivity
Musculoskeletal and connective tissue disorder	Very rare	Myalgia
General disorders and administration	Common	Fatigue
	Very rare	Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnea, pruritus, rash and urticarial)
	Not known	Asthenia
Investigations	Not known	Weight increased
Metabolism and nutrition disorders	Not known	Inceased appetite

Paediatric population
Other undesirable effects reported during the post-marketing period in paediatric patients with an unknown frequency included QT prolongation, arrhythmia, abnormal behavior (including anger, aggression and agitation) and bradycardia.

Overdose and Treatment
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.

Treatment
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.

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

Paediatric population
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.

Effects on Ability to drive and use Machine
Desloratadine 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 medical 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.

Storage Conditions
Store below 30ºC in the original package to protect from light.

Shelf Life:
3 Years

Dosage forms and packaging available
The orodispersible tablets are available in package of 1x10s tablets packed in aluminium/peelable aluminium blister.

Manufactured by:
Genepharm S.A.
18 km Marathon Avenue,
15351 Pallini Attikis,
Greece

Product Registration Holder/ Imported by:
AJ Research & Pharma Sdn. Bhd. (1014182-P)
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50088 Kuala Lumpur, Malaysia.

Product Registration No:
Ajalorin Orodispersible Tablet 2.5 mg : MAL 19016047ACZ
Ajalorin Orodispersible Tablet 5 mg : MAL 19016044ACZ

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