Summary of Product Characteristics

1. Name of the medicinal product

DESTA

2. Qualitative and quantitative composition

Each tablet contains 5 mg desloratadine.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablets

Blue, round, biconvex film-coated tablet, plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Desloratadine is indicated in adults and adolescents aged 12 years and older for the relief of symptoms associated with:- allergic rhinitis (see section 5.1), - urticaria (see section 5.1)

4.2 Posology and method of administration

Posology

Adults and adolescents (12 years of age and over)

The recommended dose of desloratadine is one tablet once a day.

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or for less than 4 weeks) should bemanaged in accordance with the evaluation of patient's disease history and the treatment could be discontinued aftersymptoms 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 theallergen exposure periods.

Pediatric population

There is limited clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age(see sections 4.8 and 5.1).

The safety and efficacy of desloratadine 5 mg film-coated tablets in children below the age of 12 years have not beenestablished.

Method of administration

Oral use.

The dose can be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1, or to loratadine.

4.4 Special warnings and precautions for use

In the case of severe renal insufficiency, desloratadine should be used with caution (see section5.2).

Desloratadine should be administered with caution in patients with medical or familial history ofseizures, and mainly young children (see section 4.8), being more susceptible to developnewseizures under desloratadine treatment. Healthcare providers may consider discontinuingdesloratadine in patients who experience a seizure while on treatment.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant interactions were observed in clinical trials with desloratadine tablets in which erythromycin orketoconazole were co-administered (see section 5.1).

Pediatric population

Interaction studies have only been performed in adults.

In a clinical pharmacology trial, desloratadine tablets taken concomitantly with alcohol did notpotentiate the performance impairing effects of alcohol (see section 5.1). However, cases of

alcohol intolerance and intoxication have been reported during post marketing use. Therefore, caution is recommended if alcohol is taken concomitantly.

4.6 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 toreproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of desloratadine duringpregnancy.

Breast-feeding

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/abstainfrom desloratadine therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for thewoman.

Fertility

There are no data available on male and female fertility.

4.7 Effects on ability to drive and use machine

Desloratadine has no or negligible influence on the ability to drive and use machines. Patientsshould 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 requiringmental alertness, such as driving a car or using machines, until they have established their own response to themedicinal product.

4.8 Undesirable effects

Summary of the safety profile

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 desloratadine were reported in 3 % of patients in excess of those treated with placebo. The most frequent of adverse reactions reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %).

Paediatric 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 DESTA
Metabolism and nutrition disorders	Not known	Increased appetite desloratadine
Psychiatric disorders	Very rare	Hallucinations
Nervous system disorders	Common Very rare	Headache Dizziness, somnolence, insomnia
Cardiac disorders	Very rare	Psychomotor hyperactivity, Tachycardia, palpitations
Gastrointestinal disorders	Common Very rare	Dry mouth Abdominal pain, nausea, vomiting
Hepatobiliary disorders	Very rare	Elevations of liver enzymes, increasedbilirubin, hepatitis

System Organ Class	Frequency	Adverse reactions seen with DESTA
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	Fatigue Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria)
Investigations	Not known	Weight increased

Pediatric population

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

A retrospective observational safety study indicated an increased incidence of new-onset seizure in patients 0 to 19 years of age when receiving desloratadine compared with periods not receiving desloratadine. Among children 0-4 yearsold, the adjusted absolute increase was 37.5

(95 % Confidence Interval (CI) 10.5-64.5) per 100,000 person years (PY) with a background rate of new onset seizure of 80.3 per 100,000 PY. Among patients 5-19 years of age, the adjusted absolute increase was 11.3 (95 % CI 2.3-20.2) per 100,000 PY with a background rate of 36.4 per 100,000 PY. (Seesection 4.4.)

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.

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 clinicaldose), no clinically relevant effects were observed.

Pediatric 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines – H1 antagonist, ATC code: R06AX27

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 ofthe expression of the adhesion molecule P-Selectin on endothelial cells. The clinical relevance of these observationsremains to be confirmed.

Clinical efficacy and safety

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 wasseen.

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 controlled clinical trials, at the recommended dose of 5 mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine 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.

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 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 effectively controlled symptoms for 24 hours.

Paediatric population

The efficacy of desloratadine 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.

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 othe rurticarial 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 thefirst 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 morethan 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 thesevariables.

5.2 Pharmacokinetic properties

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 isapproximately 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 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.

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, someinteractions 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.

Renal impaired patients

The pharmacokinetics of desloratadine in patients with chronic renal insufficiency (CRI) was compared with that ofhealthy 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 greaterin subjects with severe CRI. In both studies, changes in exposure (AUC and C_{max}) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

5.3 Preclinical 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, repeateddose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. The lack of carcinogenic potential was demonstrated in studies conducted with desloratadine and loratadine.

6. Pharmaceutical particulars

6.1 List of excipients

Tablet core:

microcrystalline cellulose, anhydrous dibasic calcium phosphate, corn starch, talc,

Tablet coating:

polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, lake indigo carmine

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store below 30 ºC, protect from excessive moisture.

6.5 Nature and contents of container

DESTA is packed 10 tablets in a blister pack (Alu-PVC) and then be closed in a secondary paper box containing 1, 6, 10 or 50 bottle (s).

Not all pack sizes may be marketed.

7.Marketing Authorization Holder

Manufactured by

Macrophar Co., Ltd.

Bangkok, Thailand

Distributed by

Macrophar Lab Co., Ltd.

28/8, Soi Pattanakarn 20 Yaek 4, Suan Luang, Bangkok, 10250 Thailand

Tel (662) 314-6671

8. Marketing Authorization Numbers

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9. Date of authorization

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10. Date of revision of the text

Sep 29, 2023