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APPROVED PACKAGE INSERT

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

DAZIT® TABLETS 5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg desloratadine.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

DAZIT® TABLETS are blue coloured circular shaped, biconvex, film-coated tablets debossed with "5" on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- **DAZIT® TABLETS** are indicated for the relief of symptoms associated with seasonal allergic rhinitis.

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- **DAZIT® TABLETS** are also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria

4.2 Posology and Method of Administration

Posology

Adults and adolescents (≥ 12 years of age): One **DAZIT® TABLET** once daily 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 patient's disease history and the treatment could be discontinued after symptoms are resolved and reinitiated upon their reappearance.

Persistent allergic rhinitis: (presence of symptoms for more than 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during allergen exposure periods).
Improvement of symptoms associated with seasonal allergic rhinitis usually becomes noticeable within 1 - 2 hours after administration of desloratadine.

Method of administration

Oral Use

DAZIT® TABLETS should be taken orally once daily with or without food:

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4.3 Contraindications

- Hypersensitivity to desloratadine or to any of the excipients listed in Section 6.1.
- Cross sensitivity to other antihistamines.

4.4. Special warnings and precautions for use

Liver impairment:

DAZIT® TABLETS should be used with caution in patients with severe liver impairment as reduced clearance of desloratadine may occur. Dosage adjustment may be needed (see section 4.2).

Renal function impairment:

A lower starting dose should be used. In patients with chronic renal impairment (creatinine clearance of 30 ml / minute or less), both oral bioavailability and peak plasma concentrations may be increased.

Epilepsy:

DAZIT® TABLETS should be administered with caution in patients with medical or familial 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.

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Weight gain:

The use of **DAZIT® TABLETS** has been associated with the risk of weight gain (see section 4.8).

Skin test:

DAZIT® TABLETS should be discontinued prior to skin tests using allergen extracts as it may inhibit the cutaneous histamine response, thus producing false-negative results. Desloratadine should be discontinued at least 48 hours before skin test.

DAZIT® TABLETS should be used with caution when the following medical conditions exists (below) and/or patients using other medication metabolised by the cytochrome P-450 system (see section 4.5) such as:

- emphysema,
- prostatic hypertrophy,
- narrow angle glaucoma,
- cardiovascular disorder,
- epilepsy or
- during acute attacks of asthma.

Safety and efficacy of **DAZIT® TABLETS** have not been established for treatment periods in excess of 4 weeks.

Special populations:

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Geriatric use:

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 with concomitant medicines.

Paediatric population:

Safety and efficacy of **DAZIT® Tablets** have not been established in paediatric patients younger than 12 years of age.

4.5-Interaction with other medicines and other forms of interaction

Cytochrome P-450 Inhibitors

Concomitant use of **DAZIT® TABLETS** with inhibitors of cytochrome P-450 enzyme system such as cimetidine, ketoconazole, clarithromycin, azithromycin and erythromycin may increase the plasma concentration (C_{max}) and area under the time concentration curve (AUC) of desloratadine as in **DAZIT® TABLETS** (see section 4.4).

Ketoconazole or Cimetidine

Reported studies relating to interactions together with desloratadine as in **DAZIT® TABLETS,** have shown, that there were no clinically relevant adverse changes in the desloratadine plasma concentrations, when ketoconazole, and/or cimetidine were used in multiple-dose interaction studies (see section 5.2).

Erythromycin or Ketoconazole

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In reported studies of clinical trials, no clinically relevant interactions were observed in with desloratadine tablets in which erythromycin or ketoconazole were co-administered (see section 5.2).

Fluoxetine

- Reports have shown that co-administration of fluoxetine with desloratadine, as contained in **DAZIT® TABLETS**, cause an increase in the C_{max} and the AUC of desloratadine and increases C_{max} of 3-OH desloratadine respectively.
- The corresponding mean parameters of norfluoxetine may be increased, with co-administration of desloratadine and fluoxetine.
- Reports of studies conducted have indicated that the C_{max} and AUC of fluoxetine may be decreased when administered with desloratadine as in DAZIT® TABLETS.

Food / Grapejuice

There was no effect of food or grapefruit juice on the disposition of desloratadine (see section 5.2).

Alcohol

As reported, in a clinical pharmacology trial study, desloratadine tablets taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol. However, cases of

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alcohol intolerance and intoxication have been reported during post-marketing use. Therefore, caution is recommended if alcohol is taken concomitantly (see section 4.8).

Paediatric population

Reports indicate that Interaction studies were only performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy in pregnancy and lactation has not been established. The use of **DAZIT® TABLETS** during pregnancy is therefore not recommended.

Breast-feeding

It has been reported that desloratadine as in **DAZIT® TABLETS** is excreted in breast milk and is therefore not recommended in breast-feeding women.

Fertility

No data has been reported on male and female fertility.

4.7 Effects on ability to drive and use machines

DAZIT® TABLETS lacks significant sedative effects effects (see section 4.8).

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Patients should, however be warned that a small number of individuals may experience sedation and blurred vision (see section 4.8). It is therefore advisable to determine individual response before driving or performing complicated tasks.

4.8 Undesirable Effects

Summary of the safety profile

In reported studies in a range of indications including allergic rhinitis and chronic idiopathic urticaria, at the recommended dose of 5 mg daily, undesirable effects with desloratadine as in **DAZIT® TABLETS** have been 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 reported study with adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this has been reported in 5,9 % of patients treated with desloratadine as in **DAZIT® TABLETS** and 6,9 % of patients receiving placebo.

Table 1: Tabulated List of Adverse Reactions

System organ class	Frequent	Less frequent	Frequency Not known
Immune system disorders	-	Anaphylaxis, angioedema, dyspnoea, urticaria,	-

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		pruritus, rash, oedema.	
Metabolism and nutrition disorders	-	-	Increased appetite
Psychiatric disorders	-	Depression, hallucinations, confusion and nightmares	Abnormal behaviour, aggression
Nervous system disorders	Headache	Fatigue, dizziness, somnolence, sedation, nervousness, insomnia, psychomotor hyperactivity, seizures.	-
Eye disorders	-	Blurred vision	-
Cardiac disorders	-	Tachycardia, palpitations,	QT prolongation
Vascular disorders	-	-	Hypotension
Blood and lymphatic system disorders	-	Blood disorders including	-

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		agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia	
Respiratory, thoracic and mediastinal disorders	Pharyngitis.	-	Dyspnoea
Gastrointestinal disorders	Dry mouth	Abdominal pain; vomiting, dyspepsia, diarrhoea, gastritis, anorexia.	-
Hepato-biliary disorders	-	Hepatitis, elevations in liver enzymes, increased bilirubin.	Jaundice
Ear and labyrinth disorders	-	-	Tinnitus
Skin and subcutaneous tissue disorders	-	Rash, alopecia	Photosensitivity
Musculoskeletal and connective tissue disorders	-	Myalgia	-

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Reproductive system and breast disorders	-	Dysmenorrhoea	-
General disorders and administration site conditions	Fatigue		Asthenia
Investigations	-	-	Weight increase

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Description of selected adverse reactions

A reported observational safety study indicated an increased incidence of new-onset seizure in patients 0 to 19 years of age when receiving desloratadine as in **DAZIT® TABLETS** compared with periods not receiving desloratadine.

There have been reports of other undesirable effects that were reported during the post-marketing period such as cases of alcohol intolerance and intoxication (see section 4.5).

Reports of cases with an unknown frequency in paediatric patients, which included QT prolongation, arrhythmia, bradycardia, abnormal behaviour, and aggression.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form” found online under SAHPRA’s publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

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

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

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.5.7.1 Antihistamines

Pharmacotherapeutic group: antihistamines - H_1 antagonist, ATC code: R06AX27

Desloratadine is the major, long acting, active metabolite of loratadine, a non-sedating tricyclic second-generation histamine (H1) antagonist.

Desloratadine exerts its action by competing with histamine for H1-receptor sites on effector cells. It prevents, but does not reverse responses mediated by histamine. Desloratadine inhibited histamine release from human mast cells in vitro. Desloratadine does not cross the blood-brain barrier to any extent.

In addition to antihistaminic properties, desloratadine has reported anti-allergic and anti-inflammatory activity from numerous in vitro and in vivo studies. These studies have been reported that desloratadine inhibits the broad cascade of events that initiate and propagate allergic inflammation.

5.2 Pharmacokinetic properties

Absorption:

Desloratadine is rapidly absorbed from the gastro-intestinal tract and reaches maximum plasma concentrations in 3 hours. Desloratadine plasma concentrations can be detected within 30 minutes of administration.

Food has no influence on the absorption of desloratadine (see section 4.2).

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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.

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 reported yet, and therefore, some interactions with other medicinal products cannot be fully excluded (see section 4.5).

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 in vivo, and in vitro studies have been reported that the medicinal product does not inhibit CYP2D6 and is neither a substrate nor an inhibitor of P- glycoprotein.

Elimination

In a reported single dose study using a 7.5 mg dose of desloratadine, there has been 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 (see section 4.5).

The mean elimination half-life of desloratadine is approximately 27 hours. Desloratadine is excreted equally in the faeces and the urine.

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5.3 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Meglumine, microcrystalline cellulose, Opadry blue 15B50612 (as coating agent), sodium starch glycolate, sodium stearyl fumarate, pregelatinised starch and starch.

Sugar free.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the bottle tightly closed.

Protect from light and moisture.

KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

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DAZIT® TABLETS are packed in white round HDPE bottle with polypropylene cap and liner. Each bottle contains 10 or 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road,

Stormill, Ext. 1, Roodepoort

Johannesburg 1724

South Africa

8. REGISTRATION NUMBER

41/5.7.1/0448

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 November 2007

8. DATE OF REVISION OF THE TEXT

28 January 2022