PROFESSIONAL INFORMATION
SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE
DAZIT® SYRUP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
DAZIT® SYRUP
Each 5 mL of DAZIT® Syrup contains 2,5 mg desloratadine.

For full list of excipients, see section 6.1
Contains sugar: Sorbitol 750 mg/5 mL and sucralose 10 mg/5 mL.

3. PHARMACEUTICAL FORM
Oral Solution
Clear, colourless solution containing 0,5 mg/mL desloratadine.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
- DAZIT®SYRUP is indicated for the relief of symptoms associated with allergic rhinitis (AR).
- DAZIT® SYRUP is also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria (CIU).

4.2. Posology and method of administration
Posology
Children 2 to 5 years of age:
2,5 mL (1,25 mg) DAZIT® SYRUP once a day, with or without a meal.
Children 6 to 11 years of age:
5 mL (2,5 mg) DAZIT®SYRUP once a day, with or without a meal.
Adults and adolescents (12 years of age and over):
10 mL (5 mg) DAZIT® SYRUP once a day, with or without a meal.
Method of administration
For Oral Use.

4.3. Contraindications
Hypersensitivity to the active substance desloratadine or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use
DAZIT® SYRUP 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.

Efficacy and safety of DAZIT® SYRUP in children under 2 years of age have not been established.

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Safety and efficacy of DAZIT® SYRUP have not been stablished for treatment periods in excess of 4 weeks for allergic rhinitis and 6 weeks for chronic idiopathic urticaria.

Renal impairment
In the case of severe renal insufficiency, DAZIT® SYRUP should be used with caution.

Paediatric population
In children below 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. The absence of upper respiratory tract infection or structural abnormalities, as well as patient history, physical examinations, and appropriate laboratory and skin tests should be considered.

Approximately 6 % of adults and children 2- to 11-year old are reported to be phenotypic poor metabolisers of desloratadine and exhibit a higher exposure. The safety of desloratadine in children 2- to 11-years of age who are poor metabolisers is reported to be same as in children who are normal metabolisers. The effects of desloratadine in poor metabolisers <2 years of age have not been reported.

Excipients

DAZIT SYRUP contains sucralose
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take DAZIT® SYRUP.

DAZIT SYRUP oral solution contains sorbitol
This medicinal product contains 150 mg sorbitol in each 1 mL of oral solution.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

Sorbitol is a source of fructose; patients with hereditary fructose intolerance (HFI) should not take this medicinal product.

DAZIT SYRUP contains propylene glycol (E1520)
This medicinal product contains 150 mg propylene glycol (E1520) in each ml of oral solution.

DAZIT SYRUP contains sodium
This medicinal product contains less than 1 mmol of sodium (6,3 mg) per 5 mL dose, that is to say it is essentially ‘sodium-free’.

4.5. Interaction with other medicines and other forms of interaction
Medicine/laboratory test interactions
Desloratadine taken concomitantly with alcohol reportedly 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.

There was no effect of food or grapefruit juice reported on the disposition of desloratadine.

It is reported that co-administration of desloratadine with ketoconazole increases the maximum desloratadine concentration (C_{max}) by 45 % and the area under the time concentration curve (AUC) by 37 %.

It is reported that co-administration of desloratadine with erythromycin increased the C_{max} of desloratadine by 24 % and the AUC by 14 %.

Co-administration of desloratadine with azithromycin reportedly resulted in an increase of both C_{max} (31 %) and AUC (12 %) of azithromycin.

The increase in C_{max} and AUC of desloratadine when co-administered with either ketoconazole or erythromycin reportedly did not cause any clinical relevant adverse events in the populations studied.

Co-administration of cimetidine with desloratadine reportedly did not significantly affect the pharmacokinetics of desloratadine.

Co-administration of fluoxetine with desloratadine reportedly caused an increase in the C_{max} of desloratadine by 15 % and an increase of 13 % in AUC and 17 % in C_{max} of 3-0H desloratadine respectively.

The C_{max} and AUC of fluoxetine were reportedly reduced by 9 % and 11 % respectively. The corresponding mean parameters of norfluoxetine increased by 23 % and 18 % respectively with co-administration of desloratadine and fluoxetine.

No clinically relevant changes in desloratadine plasma concentrations were reported in multiple-dose ketoconazole, erythromycin, azithromycin, fluoxetine and cimetidine interaction trials.

Paediatric population
Interaction studies have only been reported in adults.

4.6. Fertility, pregnancy and lactation

Pregnancy
The safe use of DAZIT® SYRUP during pregnancy has not been established. A large amount of reported data on pregnant women indicate no malformative nor foetal/neonatal toxicity of desloratadine. Reported animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. The use of desloratadine during pregnancy is therefore not recommended.

Breastfeeding
The effect of DAZIT® SYRUP on newborns/infants is unknown. Desloratadine is excreted into breast milk, therefore the use of desloratadine is not recommended in mothers who are breastfeeding their infants.

Fertility
There are no data reported on male and female fertility

4.7. Effects on ability to drive and use machines

DAZIT® SYRUP lacks significant sedative effects.

Patients should however be warned that a small number of individuals may experience sedation and dizziness. It is therefore advisable to determine individual response before driving or performing complicated tasks.

4.8. Undesirable effects

Summary of the safety profile

Paediatric population

In reported clinical trials in a paediatric population, the desloratadine as in DAZIT® SYRUP formulation was administered to a total of 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 adverse reactions reported in excess of placebo were diarrhoea (3,7 %), fever (2,3 %) and insomnia (2,3 %). In an additional reported study, no adverse events were seen in subjects between 6 and 11 years of age following a single 2,5 mg dose of desloratadine oral solution.

In a reported clinical trial with 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 reported clinical trials involving adults and adolescents in a range of indications including allergic rhinitis and chronic idiopathic urticaria, 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 summary of adverse reactions

System Organ Class	Frequency	Adverse reactions seen with Desloratadine
Metabolism and nutrition disorders	Not known	Increased appetite
Immune system disorders	Less frequent Not known	Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria) Asthenia
Psychiatric disorders	Less frequent Not known	Hallucinations Abnormal behaviour, aggression
Nervous system disorders	Frequent Frequent (children less than 2 years) Less frequent	Headache Insomnia Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Less frequent Not known	Tachycardia, palpitations QT prolongation
Gastrointestinal	Frequent	Dry mouth

disorders	Frequent (children less than 2 years) Less frequent	Diarrhoea Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea
Hepatobiliary disorders	Less frequent Not known	Elevations of liver enzymes increased bilirubin, hepatitis Jaundice
Skin and subcutaneous tissue disorders	Not known	Photosensitivity
Musculoskeletal and connective tissue disorders	Less frequent	Myalgia
General disorders and administration site conditions	Frequent Frequent (children less than 2 years)	Fatigue Fever
Investigations	Not known	Weight increase

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

A reported retrospective 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® SYRUP compared with periods not receiving desloratadine. Among children 0-4 years old, 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 3,4 per 100,000 PY.

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 Reaction Reporting form'**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/index/8.

4.9. Overdose
The adverse event profile associated with overdosage, as reported during post-marketing use, is similar to that reported 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 reported multiple dose clinical trial in adults and adolescents, in which up to 45 mg of desloratadine was administered (nine times the clinical dose), no clinically relevant effects were observed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.5.7.1 Anitihistamines

Pharmacotherapeutic group: antihistamines – H_1 antagonist, ATC code: R06AX27
Mechanism of action:
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. It does not readily penetrate into the central nervous system.

In addition to antihistaminic activity, desloratadine has demonstrated anti-allergic and anti-inflammatory activity from numerous reported *in vitro* (mainly conducted on cells of human origin) and *in vivo* studies. These studies have shown that desloratadine inhibits the broad cascade of events that initiate and propagate allergic inflammation.

5.2. Pharmacokinetic properties

Absorption
Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine 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 has been reported to be consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. In adults and adolescents, the bioavailability of desloratadine has been reported to be dose proportional over the range of 5 mg to 20 mg.
In separate reported single dose studies, at the recommended doses, paediatric patients had comparable AUC and C_{max} values of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Distribution
Desloratadine is moderately bound (83 % - 87 %) to plasma proteins. There is no reported evidence of clinically relevant drug 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 drugs cannot be excluded. Reported *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 or CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

Elimination
In a reported single dose crossover trial using a 7,5 mg dose of desloratadine, the tablet and syrup formulations were bioequivalent and not effected by the presence of food (high-fat, high caloric breakfast). In another reported study, grapefruit juice had no effect on the disposition of desloratadine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Hypromellose, sucralose, citric acid, sodium citrate, liquid (non-crystallising) sorbitol, propylene glycol, liquid tutti frutti flavour, purified water.
6.2 Incompatibilities
Not applicable
6.3 Shelf life
36 months
6.4 Special precautions for storage
Store at or below 30 °C. Protect from light.
Store in the original container
KEEP OUT OF REACH OF CHILDREN.
6.5 Nature and contents of container
Amber glass type III bottles of 100 mL and 150 mL closed with a white plastic child-resistant screw cap. The bottles are packed in cardboard boxes, and a measuring (device) spoon marked for doses of 2,5 mL and 5 mL is included in the secondary packaging.
6.6 Special precautions for disposal and other handling
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
RANBAXY PHARMACEUTICALS (PTY) LTD
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8. REGISTRATION NUMBER
57/5.7.1/0264

9 DATE OF FIRST AUTHORISATION
16 May 2023

10. DATE OF REVISION OF THE TEXT

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