SCHEDULING STATUS

S2

1. **NAME OF THE MEDICINE:**

   AVARINEX SYRUP

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION:**

   Active substance: Desloratadine

   Each 5 mL of AVARINEX syrup contains 2.5 mg of desloratadine.

   Contains sugar: Sucrose 2,5 mg

   Contains sorbitol 1400 mg

   Contains propylene glycol 500 mg

   Contains preservative: Sodium benzoate 5 mg

   For the full list of excipients, see **section 6.1**

3. **PHARMACEUTICAL FORM:**

   AVARINEX SYRUP:

   Orange coloured, clear liquid having an orange flavour.

4. **CLINICAL PARTICULARS:**

   4.1 Therapeutic Indications

   AVARINEX Syrup is indicated for the relief of symptoms associated with allergic rhinitis (AR).

   AVARINEX Syrup is also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria (CIU).

   4.2 Posology and method of administration

   Children 2 to 5 years of age:

2.5 mL (1.25 mg) AVARINEX Syrup once a day.

Children 6 to 11 years of age:

5 mL (2.5 mg) AVARINEX Syrup once a day.

Adults and adolescents (12 years of age and over):

10 mL (5 mg) AVARINEX Syrup once a day.

Patients with hepatic or renal impairment should be given 5mg **AVARINEX** on alternate days initially.

If the child is less than 5 years old, enquire if the child is using other medicines that contain propylene glycol or alcohol.

Method of administration

For oral use

The dose can be taken with or without a meal.

4.3 Contraindications

- Hypersensitivity to desloratadine or to any of the excipients listed in section 6.1.
- Pregnancy and lactation (see section 4.6).
- Cross sensitivity to other antihistamines
- Porphyria

4.4 Special warnings and precautions for use

Seizures

Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children (see section 4.8), being more susceptible to develop new seizures under desloratadine treatment.

Efficacy and safety of desloratadine syrup have not been established for treatment periods in excess of 4 weeks.

Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Special populations

Renal and hepatic function impairment

Patients with hepatic or renal impairment should begiven 5mg AVARINEX on alternate days initially.

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 phenotypic poor metabolisers of desloratadine and exhibit a higher exposure (see section 5.2). The safety of desloratadine in children 2- to 11-years of age who are poor metabolisers is the same as in children who are normal metabolisers. The effects of desloratadine in poor metabolisers < 2 years of age have not been studied.

AVARINEX syrup should be discontinued prior to skin tests allergen extracts as it may inhibit the cutaneous histamine response, thus producing false-negative results. **AVARINEX** syrup should be discontinued at least 48 hours before test.

AVARINEX contains:

Sucrose

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Propylene Glycol

This medicine contains 500 mg propylene glycol in each 5 mL which is equivalent to 20-25 mg/kg body weight.

Sorbitol Solution

Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

4.5 Interaction with other medicines and other forms of interaction

No clinically relevant changes in desloratadine plasma concentrations were observed in multiple-dose ketoconazole, erythromycin, azithromycin, fluoxetine and cimetidine interaction trials. (see section 5.1).

Paediatric population

Interaction studies have only been performed in adults.

Desloratadine syrup taken concomitantly with alcohol did not potentiate 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.

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

4.6 Fertility, pregnancy, and lactation

Pregnancy

A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicates no malformative nor foeto/ neonatal toxicity of desloratadine. **AVARINEX** should not be used during pregnancy see section 4.3

Breast-feeding

Desloratadine has been identified in breastfed newborns/infants of treated women. The effect of desloratadine on newborns/infants is unknown. Avarinex is not recommended for use during breastfeeding.

Fertility

There are no data available on male and female fertility

4.7 Effects on the ability to drive and use machines

AVARINEX Syrup lacks significant sedative effects.

Patients should however be warned that a small number of individuals may experience sedation. 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

The overall incidence of adverse events in children 2 through 11 years of age was found to be similar for the desloratadine and placebo groups, in clinical trials. 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 clinical trial with adolescent patients, 12 through 17 years of age, the most common adverse event was headache.

Adults and adolescents

The most frequent of adverse events reported in excess of placebo were fatigue, dry mouth and headache.

Metabolism and nutrition disorders

Frequency unknown: Increased appetite

Psychiatric disorders

Less frequent: Hallucinations

Frequency Unknown: Abnormal behaviour, aggression

Nervous system disorders

Frequent: Headache, insomnia

Less frequent: Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures

Cardiac disorders

Less frequent: tachycardia, palpitations

Frequency unknown: QT prolongation

Gastrointestinal disorders

Frequent: Dry mouth, diarrhoea

Less frequent: Abdominal pain, nausea, vomiting, dyspepsia,

Hepatobiliary disorders

Less frequent: Elevations of liver enzymes, increased bilirubin, Hepatitis

Frequency unknown: Jaundice

Skin and subcutaneous tissue disorders

Less frequent: Photosensitivity

Musculoskeletal and connective tissue disorders

Less frequent: Myalgia

General disorders and administration site conditions

Frequent: Fatigue, fever

Less frequent: Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria)

Frequency unknown: Asthenia

Investigations

Frequency unknown: weight increased

Paediatric population

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

Reporting side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of 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: hppts://www.sahpra.or.za/Publications/Index/8

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 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

CATEGORY AND CLASS

A.5.7.1 Antihistaminics

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 of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.

5.2 Pharmacokinetic properties

Absorption

Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine administration in adults and adolescents. 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.

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. Similar pharmacokinetic parameters were observed in a multiple-dose pharmacokinetic study conducted with the syrup formulation in paediatric poor metaboliser subjects 2- to 11-year old diagnosed with allergic rhinitis. The exposure (AUC) to desloratadine was about 6-fold higher and the Cmax was about 3 to 4 fold higher at 3-6 hours with a terminal half-life of approximately 120 hours. Exposure was the same in adult and paediatric poor metabolisers when treated with age appropriate doses. The overall safety profile of these subjects was not different from that of the general population. The effects of desloratadine in poor metabolisers < 2 years of age have not been studied. In separate single dose studies, at the recommended doses, paediatric patients had comparable AUC and Cmax 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 evidence of clinically relevant active substance accumulation following once daily adult and adolescent dosing of desloratadine (5 mg to 20 mg) for 14 days. In a single dose, crossover study of desloratadine, the tablet and the syrup formulations were found to be bioequivalent.

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.

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.

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.

6. Pharmaceutical particulars

6.1 List of excipients

Beta cyclodextrin, citric acid anhydrous, disodium EDTA, glycerin, orange flavour, polyvinyl pyrrolidone, propylene glycol, sodium benzoate, sodium citrate, sorbitol solution, sucralose, sunset yellow.

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 °C in original container.

6.5 Nature and contents of container

AVARINEX syrup:

Is packaged in a 60 mL or 100 mL or 150 mL PET bottle, with a PP cap in an outer carton with package insert.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements

7. Holder of certificate of registration

Innovata Pharmaceuticals

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

South Africa

8. Registration numbers

A 57/5.7.1/0168

9. Date of first authorization/Renewal of the authorization

29/01/2025

10. Date of revision of the text

05/08/2025